UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

For Annual and Transition Reports Pursuant to Sections 13 or 15(d) of the Securities Exchange Act of 1934

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the Fiscal Year Ended December 31, 2002

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Commission File Number: 0-27352

HYBRIDON, INC.

(Exact name of Registrant as specified in its certificate of incorporation)

Delaware	**04-3072298**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
345 Vassar Street Cambridge, Massachusetts	**02139**
(Address of principal executive offices)	**(Zip Code)**

(617) 679-5500
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act: None

Securities registered pursuant to Section 12(g) of the Act:

Common Stock, $.001 par value
(Including Associated Preferred Stock Purchase Rights)
(Title of Class)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to the filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

Indicate by check mark whether the registrant is an accelerated filer (as defined in Exchange Act Rule 12b-2). Yes ☐ No ☒

The approximate aggregate market value of the voting stock held by non-affiliates of the registrant was $46.1 million as of June 28, 2002. As of March 7, 2003, the registrant had 43,456,045 shares of Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Proxy Statement with respect to the Annual Meeting of Stockholders to be held on June 19, 2003	Items 10, 11, 12 and 13 of Part III.

HYBRIDON, INC.

FORM 10-K

INDEX

PART I.

Item 1. *Business*

Overview

We are a leading company in the discovery and development of novel therapeutics and diagnostics using synthetic DNA. Our activities are based on four technologies:

- Our immunomodulatory oligonucleotide, or IMO, technology uses synthetic DNA that contains specific sequences that mimic bacterial DNA to modulate responses of the immune system. We have designed a class of IMO compounds, which we refer to as 2nd generation IMO compounds, that we believe may offer potential advantages over earlier immunostimulatory oligonucleotides. These earlier immunostimulatory oligonucleotides are generally referred to in the industry as CpG DNA because they contain a segment of DNA consisting of a cytosine (C) molecule and a guanine (G) molecule linked by a phosphorous bond (p). We are designing our IMO compounds to be used as monotherapies in the treatment of conditions such as cancer, infectious diseases and allergic asthma and other allergies, as well as in combination therapies with chemotherapeutics, vaccines and antibodies.

- Our antisense technology uses synthetic DNA to block the production of disease causing proteins at the cellular level. We have developed advanced antisense chemistries that serve as the basis for our 2nd generation antisense drug candidates. We believe that these 2nd generation drug candidates may offer potential advantages over earlier antisense drug candidates and are potentially applicable to a wide variety of therapeutic indications. We are currently focusing our internal antisense efforts on cancer and infectious diseases. In addition, we are collaborating with other companies to develop antisense therapeutics in the areas of cancer, infectious diseases and pulmonary disease.

- Our cancer therapy potentiation technology uses synthetic DNA to enhance the antitumor activity of certain marketed anticancer drugs and increase their effectiveness. This technology is based on our discovery in preclinical studies that when oligonucleotides are administered in combination with specific marketed anticancer drugs, such as irinotecan which is marketed in the United States under the name Camptosar®, the activity of the co-administered anticancer drug is greatly improved.

- Our Cyclicon technology uses novel synthetic DNA structures, which we refer to as Cyclicons, for identifying gene function in drug target validation and drug discovery.

Lead Products. In the near term, we are focusing our internal drug development efforts on developing the two lead drug candidates in our pipeline, HYB2055 and GEM231.

- HYB2055 is the lead clinical drug candidate in our IMO program. We are evaluating HYB2055 for the treatment of solid tumor cancers. The Investigational New Drug Application, or IND, we submitted to the United States Food and Drug Administration, or FDA, covering HYB2055 became effective on March 6, 2003. In March 2003, we commenced a phase 1 trial of HYB2055 in the United Kingdom in healthy volunteers. We anticipate commencing a phase 1 trial of HYB2055 in the United States in cancer patients during the second quarter of 2003.

- GEM231 is a 2nd generation antisense compound for treating solid tumor cancers. GEM231 is designed to inhibit Protein Kinase A, or PKA, a protein whose levels have been shown to be increased in the cells of many human cancers. We are currently conducting a phase 1/2 clinical trial of GEM231 as a combination therapy with Camptosar. We plan to commence a phase 2 trial using this drug combination in the second half of 2003 based upon pharmacokinetic analysis and other data obtained from the ongoing phase 1/2 trial.

Collaboration Strategy. In addition to developing drug candidates on our own, we are seeking alliance partners to collaborate on products based on both our IMO and antisense technologies. We believe that pharmaceutical and biotechnology companies may seek to combine our IMO compounds with their chemotherapeutics, vaccines and monoclonal antibodies.

We also believe our antisense technology may prove useful to pharmaceutical and biotechnology companies that are seeking to develop antisense drug candidates to down-regulate gene targets discovered by, or proprietary to, such companies. We have already entered into six licensing agreements for our antisense technology and are seeking to enter into additional agreements for both our IMO and antisense technologies.

Recent Developments

In 2002 and the first quarter of 2003, we continued the development of our technologies, advanced our product pipeline, strengthened our management team and board of directors, and entered into licensing and development collaborations.

HYB2055 Investigational New Drug Application. The IND we submitted to the FDA covering HYB2055 became effective on March 6, 2003. In March 2003, we commenced a phase 1 clinical trial of HYB2055 in the United Kingdom in healthy volunteers.

Expansion of our Management Team and New Board Members. In 2002, we supplemented our management team by filling important open positions. We hired a senior director of our preclinical drug development program, a director of business development and a director of scientific affairs. We also added two new members to our board of directors, William S. Reardon, CPA and Georges Anthony Marcel, M.D., PhD.

Mr. Reardon is a retired audit partner from PricewaterhouseCoopers LLP, where he led the Life Science Industry Practice for New England and the Eastern United States. He worked with numerous life science companies, including Genzyme Corp., Vertex Pharmaceuticals, Inc., Sepracor Inc. and Cubist Pharmaceuticals, Inc. Mr. Reardon has also served on the Board of the Emerging Companies Section of the Biotechnology Industry Organization and the Board of Directors of the Massachusetts Biotechnology Council.

Dr. Marcel is currently President of TMC Development, a biotechnology consulting firm whose clients include biotechnology corporations and institutional investors. Dr. Marcel's previous experience includes roles as President and Chief Executive Officer of the French subsidiary of Amgen, Inc. and Chief Executive Officer of Laboratoires Roussel. Dr. Marcel is a member of the Gene Therapy Committee of the French Medicines Agency, which is the French equivalent of the FDA. He is also a member of the Board of St. Honore Vie et Sante, a health care investment fund of the Rothschild Group; a member of the Board of the French Genopole Premier Jour, an entity sponsored by the French government to provide seed capital to emerging biotechnology companies; and a member of the Board of Pharmos Corporation.

New Collaboration and License Agreements. In September 2002, we entered into two new collaboration and license agreements:

- *Aegera Therapeutics Inc.* Our agreement with Aegera relates to the development of an antisense drug targeted to the XIAP gene, a gene which has been implicated in the resistance of cancer cells to chemotherapy.
- *Micrologix Biotech, Inc.* Our agreement with Micrologix relates to the development of an antisense drug for the treatment of human papillomavirus.

Amendment to Isis Collaboration and License Agreement. In August 2002, we amended our collaboration and license agreement with Isis Pharmaceuticals, Inc. The amendment limited each party's obligation to participate in collaboration committee meetings and terminated the obligations of each party to make the remaining installment payments due from each party under the agreement. As a result of the amendment, in the third quarter of 2002 we recognized revenue and expenses of approximately $27.9 million and $2.1 million, respectively, that we had previously deferred.

Our Product Pipeline

The table below summarizes the principal products we are developing independently or in collaboration with third parties and the therapeutic use and development status of these products.

Product Description	Therapeutic Use	Development Status
IMO™		
HYB2055 — 2nd generation IMO	Cancer	phase 1
Antisense		
GEM231 — 2nd generation antisense drug candidate targeted to PKA	Cancer	phase 1/2
GEM92 — 2nd generation antisense drug candidate targeted to a specific region of HIV-1	HIV	phase 1
MBI 1121 — 2nd generation antisense drug candidate targeted to HPV[1]	Human Papillomavirus	phase 1
GEM220 — 2nd generation antisense drug candidate targeted to Vascular Endothelial Growth Factor	Cancer	preclinical candidate
GEM240 — 2nd generation antisense drug candidate targeted to MDM2	Cancer	preclinical candidate
GEM640 (AEG35156) — 2nd generation antisense drug candidate targeted to XIAP[2]	Cancer	preclinical candidate
Cancer Therapy Potentiation		
GEM231 — 2nd generation antisense drug candidate used to potentiate the antitumor activity of Camptosar	Cancer	phase 1/2

1. Being developed by Micrologix Biotech, Inc. in collaboration with us.

2. Being developed by Aegera Therapeutics, Inc. in collaboration with us.

Immunomodulatory Oligonucleotide (IMO™) Technology

Overview

Our IMO technology has evolved from our research experience with antisense oligonucleotides. We have learned from this research experience that some types of oligonucleotides can act as potent stimulators of the immune system. Our early insights and those of others showed that oligonucleotides containing specific nucleotide segments or motifs mimic in the human body the immune stimulating effects of bacterial DNA. Nucleotides are the molecules that are linked together to form DNA. Using our DNA chemistry, we have designed and are developing a new, proprietary class of IMO compounds. We believe these compounds, which we refer to as 2nd generation IMO compounds, may offer a number of potential advantages over earlier immunostimulatory oligonucleotides, including:

- greater potency;
- greater specificity because 2nd generation IMO compounds can be designed to induce different aspects of the human immune system;
- reduced manufacturing costs; and
- the possibility of composition of matter patent protection.

We are designing our IMO compounds to be used as monotherapies in the treatment of conditions such as cancer, infectious diseases and allergic asthma and other allergies, as well as in combination therapies with chemotherapeutics, vaccines and antibodies.

Background

The human immune system protects the body against viruses, bacteria and other infectious agents, referred to as pathogens. It also acts to identify and eliminate abnormal cells, such as cancer cells. The immune system acts through various mechanisms which recognize pathogens and abnormal cells and initiate a series of interactions that activate specific genes to respond to pathogens or abnormal cells. The immune system is made up of two parts: the innate immune system and the adaptive immune system.

The role of the innate immune system is to provide a rapid, non-specific response to a pathogenic invasion or to the presence of a foreign substance in the body. The innate immune system consists of cells such as macrophages, dendritic cells and monocytes. When the body is presented with a pathogen, cells of the innate immune system are activated, resulting in a cascade of signaling events which cause the production of proteins to fight the infection. Unlike the antibodies and proteins produced by the adaptive immune system described below, the proteins produced by the innate immune system are not pathogen-specific, but rather are active against a broad spectrum of pathogens. Moreover, once the infection is resolved, the innate immune system will not remember the pathogen.

The adaptive immune system provides a highly effective, pathogen-specific response to a pathogenic invasion. The adaptive immune system does this by recognition of specific cell surface proteins, called antigens, which signal the presence of a pathogen. This process is initiated through signals produced by the innate immune system. Upon recognition of an antigen, the adaptive immune system produces antibodies and antigen-specific toxic immune cells that specifically detect and destroy infected cells. This response is referred to as an antigen-specific immune response. An antigen-specific immune response normally takes several weeks to develop the first time. However, once challenged by a pathogen, the adaptive immune system remembers the antigens of the pathogen. In this manner, if the pathogen again invades the body, the presence of the remembered antigens will allow the adaptive immune system to respond once again, this time in a matter of days. Scientists believe that the adaptive immune system can eliminate abnormal cells, such as cancer cells.

The immune reaction in vertebrates, including humans, is first commenced by activation of the innate immune system. One way this is achieved is by the recognition of a pathogen-associated molecular pattern, referred to as a PAMP. These patterns include components of DNA that are present with great frequency in pathogens and with low frequency, or not at all, in vertebrates. The presence of a PAMP acts as a signal to the immune system of the presence of a foreign pathogen.

In the case of bacteria, one common PAMP is a combination of two of the components, or building blocks, of DNA known as the CpG dinucleotide or CpG DNA. Most bacteria contain this CpG motif at the expected frequency of one in sixteen base pairs in their genome. Vertebrates display many fewer CpG dinucleotides, and usually the cytosine (C) molecule of the CpG motif is methylated, unlike bacterial CpG dinucleotides where the cytosine (C) molecule is unmethylated. In this way self DNA is not mistaken for pathogen DNA. Methylation is the substitution of a methyl group, a molecule containing one carbon atom and three hydrogen atoms, for a hydrogen atom.

CpG DNA has been shown to be recognized by a specific protein receptor called toll-like receptor 9, or TLR9. This receptor is on the surface or inside of the immune cells. Scientists generally believe that once TLR9 recognizes bacterial DNA such as CpG DNA, TLR9 triggers an immune response through a cascade of cell signals that ultimately lead to the release of immune system molecules that attack the infection. Additional receptors may also contribute to or modify the recognition of certain CpG DNA, emphasizing the structural importance of CpG DNA in TLR-specific signaling.

Our IMO compounds are synthetic CpG-like DNA that contain specific sequences that mimic bacterial DNA. We believe these sequences are recognized as bacterial DNA by TLR9 and other receptors. As a result, IMO compounds trigger an innate immune response similar to the innate immune response triggered by bacterial DNA. Preclinical studies of our IMO compounds have shown that this response leads to signaling events that include production of cytokines, which are a specific type of immune system molecule, and are known to have broad spectrum therapeutic properties against infectious disease as well as against cancer. In addition, signals from the innate immune system may trigger responses of the adaptive immune system. This

recognition of IMO compounds by TLR9 or other receptors may also allow the use of IMO compounds in combination with vaccines, antigens, and allergens used to treat a number of diseases.

Therapeutic Potential of IMO™ Compounds

Because IMO compounds generate immune responses, we believe that they may provide therapeutic benefits in a number of areas:

- *Cancer.* Cancer cells are recognized by the body as abnormal cells and trigger an immune response. However, this response is notoriously weak. The benefits of immunostimulation by bacterial DNA in cancer patients have been long recognized. We believe that IMO compounds may strengthen the immune response to cancer cells. In preclinical studies in animals, IMO compounds have been shown to delay tumor growth.
- *Allergic Asthma and other Allergies.* The type of cytokines, which are products of white blood cells, produced as a result of the activation of immune cells by IMO compounds suppress asthmatic and allergic immune conditions while simultaneously promoting an immune response that further alleviates asthmatic and allergic conditions. Based on preclinical studies of our IMO compounds, we believe that IMO compounds have potential for use in the treatment of allergic asthma, other allergies and other diseases which result from an overreaction of the immune system.
- *Infectious Diseases.* In published reports, CpG DNA have been shown to activate an immune defense against pathogens that is of a general nature and not directed at any specific microorganism. As a result, we believe IMO compounds have the potential to be used prophylactically to ward off the danger of infection or to boost the immune response to an early-stage or ongoing infection.
- *Combination with Vaccines.* We believe IMO compounds have the potential to be used in combination with vaccines or antibody therapies. In preclinical studies the immune response triggered by IMO compounds increased the production of specific antibodies.

IMO™ Chemistry

Preclinical studies have demonstrated that exposure of IMO compounds to various blood cells induces the expression of many cytokines. These studies also showed that the mechanism of cytokine production by IMO compounds is complex and varies somewhat from one oligonucleotide to another. In particular, effects vary depending on the sequence and structure of the IMO.

Based on our extensive experience with DNA chemistry, we are developing 2nd generation IMO compounds which in cell culture and mice have shown improved immunomodulatory properties compared with 1st generation immunostimulatory compounds, such as CpG DNA. Our 2nd generation IMO compounds contain specific nucleotide sequences which we have designed to have different effects on the immune system. We refer to compounds with the specific sequences containing the immunomodulatory motifs and modifications as YpG, CpR, and YpR IMO compounds based on the particular motifs contained in them. We are designing these 2nd generation IMO compounds to be more potent than 1st generation immunostimulatory compounds as well as to induce the specific cytokines appropriate for treatment of different diseases. As a result we have the ability to create a portfolio of 2nd generation IMO compounds that can provide different custom-designed drug candidates for a variety of therapeutic or prophylactic uses.

HYB2055 Drug Discovery and Development

In 2002, we selected HYB2055 as the lead preclinical candidate in our IMO program. We selected HYB2055 because of the potency it demonstrated as an immune modulator in preclinical models, both *in vitro* and *in vivo*. We submitted an IND for HYB2055 on February 4, 2003, which became effective on March 6, 2003. Our first clinical program for HYB2055 will be for use as a monotherapy in the treatment of cancer. In March 2003, we initiated a phase 1 clinical trial in England to study the safety of HYB2055 in healthy volunteers. We anticipate commencing a phase 1 trial in the United States in cancer patients in the second

quarter of 2003. We believe HYB2055 also may have use as part of a combination therapeutic regimen with chemotherapeutics.

In addition to cancer, we believe the IMO compound used in HYB2055 could also have use as a monotherapy for treatment of allergic asthma and other allergies and infectious diseases, as well as in combination with vaccines and monoclonal antibodies. We intend to explore the potential of these uses either on our own, or with collaborators, but each such use would be subject to the submission of additional INDs prior to the commencement of any clinical trial.

Antisense Technology

Introduction

The heart, brain, liver and other organs in the human body function together to support life. Each microscopic cell within these organs produces proteins that affect how that cell functions within the organ, and ultimately how efficiently each organ functions within the body.

A normal cell produces a given set of normal proteins in the right amount for the body to function properly. A diseased cell produces inappropriate or mutant proteins, or produces the wrong amount of normal proteins. A cell produces inappropriate types or amounts of proteins when its DNA expression changes, either through mutation, as in many types of cancer cells, or by infection with a virus. In some instances, inappropriate proteins act directly to cause or support a disease. In other instances, inappropriate proteins interfere with proteins that prevent or combat disease. Most traditional drugs are designed to interact with and inhibit the function of protein molecules that are already present in the body and causing or supporting disease. In contrast, antisense technology permits the design of drugs that intervene at the earlier genetic level to inhibit production of disease-causing or disease-supporting proteins.

The full complement of human genes, known as the human genome, contains the information required to produce all human proteins. A copy of the complete human genome is present in each cell, and each cell makes proteins based on its copy of the genome. The information that controls a cell's production of a specific protein is contained in the gene relating to that protein. Each gene is made up of two intertwined strands of DNA that form a structure called a "double helix." Each strand of DNA consists of a string of individual DNA building blocks called nucleotides, arranged in a specific sequence. It is the sequence of nucleotides that contains genetic information. One of the paired strands of the double helix contains the information that directs the composition of a specific protein, and is called the "coding" strand. The other strand, the "non-coding" strand, contains a different but complementary sequence of nucleotides.

Cells make proteins in a two-stage process. First, the cell creates a molecule of messenger RNA consisting of a string of nucleotides in a sequence that is the exact mirror image of, or complementary to, the sequence of the coding strand of DNA in the double helix. This messenger RNA strand is called the "sense" sequence. In the next step, the cell produces proteins based on the information contained in the messenger RNA.

Conventional Drugs

Most drugs are chemicals that stimulate or suppress the function of a particular molecule, usually a protein, which causes a disease. The drug acts by binding to the target molecule, often at as few as two or three points of contact with the target molecule. Once the binding takes place, the disease-causing activity of the target molecule is interrupted.

Frequently, however, sites on other non-target molecules present in the body resemble the target-binding site of a disease-causing molecule enough to permit the conventional drug to bind to some degree to those non-target molecules. Most drug side effects arise due to this drug interaction with molecules other than the target molecule. This lack of selectivity can result in unwanted side effects, potentially requiring lower doses of the drug, and thus, decreasing effectiveness.

Another characteristic of conventional drugs is that developing them is a time-consuming and expensive process. For every compound that is found to be effective and have tolerable side effects, thousands may be investigated and rejected. In the traditional drug discovery process, this may take many years and millions of dollars.

Antisense Drugs

A synthetic DNA molecule with a sequence exactly complementary to the sense sequence of the messenger RNA of a specific gene can bind to and inhibit the function of that messenger RNA. This exact complement of the sense messenger RNA sequence is referred to as an antisense sequence or oligonucleotide. By inhibiting the function of the relevant messenger RNA, it is possible to decrease or eliminate the production of disease-causing or disease-supporting proteins. Moreover, the nucleotide sequence of an antisense synthetic DNA complementary to its target sequence on the messenger RNA can be designed in a manner such that the antisense synthetic DNA forms a large number of bonds at the target site, typically 30 or more, as compared to as few as two to three bonds for conventional drugs. This allows the oligonucleotide to form a strong bond with the messenger RNA.

Antisense drug development technology involves the design and synthesis of synthetic DNA to bind and inhibit the activity of messenger RNA which codes for the production of disease-associated proteins. We believe that drugs based on antisense technology may be more effective and cause fewer side effects than conventional drugs because antisense drugs are designed to intervene in a highly specific fashion in the production of proteins, rather than after the proteins are made. Moreover, in contrast with small molecule drug discovery which may take many years, once a gene target has been identified an antisense drug candidate can be designed in about 90 days.

Recent years have seen a dramatic increase in the understanding of the role of genes in producing proteins associated with disease. This knowledge has come from many sources, including the human genome project and the work being done by academic institutions and pharmaceutical companies all over the world. As a consequence, we believe that the pharmaceutical industry is increasingly becoming an environment that is rich in potential drug targets. The challenge for the future will be to create drugs effective against these newly discovered gene targets. We believe that the increase in the number of potential targets provides us with increasing opportunities to employ our antisense technology. Once a gene associated with a disease-associated protein is identified, it should be possible to design a synthetic DNA with an antisense mechanism designed to stop production of that protein and to improve the pharmaceutical effects of that synthetic DNA by chemical modification.

Hybridon Antisense Technology

We were founded in 1989 to exploit the pioneering work of Paul Zamecnik, M.D., a member of our board of directors, who is regarded by many as the father of antisense. We are a leader in the antisense field, particularly in the key area of developing the novel chemical structures on which advanced, or 2nd generation, antisense drug candidates are based.

Our antisense technology is based on our advanced chemistries, which enable us to alter the chemical makeup of the backbone of a synthetic DNA compound in a manner designed to make the compound safer and more stable than the backbone of synthetic DNA developed using 1st generation antisense chemistry and to do so without adversely affecting the compound's ability to inhibit the production of disease-associated proteins. A DNA backbone is the linkage between the sugars and bases known as nucleosides that form a strand of DNA. Oligonucleotides which contain a natural backbone are not suitable for use as drugs because they are rapidly degraded by enzymes before they reach the intended target.

In order to increase the stability of oligonucleotides against these enzymes, we have developed oligonucleotides which are chemically modified by replacing certain oxygen atoms on the backbone with sulfur atoms. We refer to oligonucleotides with this modification as 1st generation antisense compounds. 1st generation antisense compounds have been shown to have increased stability and in limited cases to be effective drugs. One of our competitors in the antisense field currently markets a 1st generation antisense drug

to treat a viral infection through local delivery. Two other 1st generation antisense drugs are in late-stage clinical trials for cancer. However, we believe that these 1st generation compounds have limited pharmaceutical utility because, despite the chemical modification, these compounds are relatively toxic, degrade in the human body quickly and are not well suited for oral administration.

We have designed and created families of advanced synthetic DNA chemistries, including DNA/RNA combinations, called hybrid or mixed backbone compounds. The results of our preclinical studies and our GEM231 phase 1 clinical trials in over 80 patients have suggested that by modifying the synthetic backbone of our 1st generation antisense compounds with different combinations of our advanced chemistries, we can improve the properties of 1st generation antisense compounds to make them more effective agents for multiple applications. In particular, we believe that antisense compounds based on these advanced chemistries, which we refer to as 2nd generation antisense compounds, will show favorable pharmaceutical characteristics and significantly improved therapeutic utility as compared to 1st generation antisense compounds. We believe that 2nd generation antisense compounds may exhibit the following desirable characteristics in comparison with 1st generation compounds:

- fewer side effects;
- greater stability in the body, enabling patients to take doses less frequently;
- greater potency, permitting patients to take lower doses; and
- greater potential for multiple routes of administration, including by injection, orally or topically.

Antisense Drug Development and Discovery

Because antisense technology works at a genetic level, it is well suited for functional genomics, drug discovery and validation of therapeutic drug targets, and ultimately for bringing new drug therapies to the market. We believe that our antisense technology is potentially applicable to a wide variety of therapeutic indications, including cancer, viral and infectious disease, autoimmune and inflammatory disease, respiratory diseases, cardiovascular disease and diabetes because these diseases are often caused by the over production of proteins which may be down regulated by antisense oligonucleotides. We are focusing our drug development and discovery efforts on developing 2nd generation antisense drugs for cancer and infectious diseases. We currently have two antisense compounds in the clinical phase of development and a number of other compounds in preclinical development.

Clinical Development

GEM231 for the Treatment of Cancer. GEM231 is a 2nd generation antisense compound for treating solid tumor cancers. We are currently conducting a phase 1/2 clinical trial of GEM231 as a combination therapy with Camptosar. We chose to evaluate the combination of GEM231 and Camptosar based on promising preclinical data relating to this combination as a treatment of solid tumor cancers.

We are conducting the phase 1/2 trial at Vanderbilt University Medical Center and the University of Chicago Medical Center. In the clinical trial, we are evaluating the safety of GEM231 and Camptosar in combination and measuring the presence of extra-cellular PKA, or ECPKA, in blood as a biomarker for GEM231 antisense activity. A biomarker is a biological parameter monitored as a possible indicator of drug activity.

GEM231 is designed to inhibit protein kinase A, or PKA. PKA is a protein that plays a key role in the control of the growth and differentiation of mammalian cells. Levels of PKA have been shown to be increased in the cells of many human cancers, and high levels of PKA have been shown to correlate with unfavorable clinical outcomes in patients with breast, colon and ovarian cancers.

We previously conducted other phase 1/2 clinical trials of GEM231, both as a monotherapy and in combination with other marketed chemotherapeutics. We believe that these trials involved the first systemic administration of a 2nd generation antisense compound to oncology patients. In December 2002, we completed a phase 1/2 study of 14 patients with solid tumors undergoing treatment with GEM231 as a

monotherapy. In the study, ECPKA was monitored for each patient before and during the treatment as a biomarker for GEM 231 activity. Results of the study showed a decrease in ECPKA in patients.

In the Phase 1/2 trial of GEM231 as a monotherapy and in our other trials of GEM231, we also evaluated the safety of GEM231 in multiple doses in oncology patients. These trials explored the maximum tolerated dose of GEM231 for both single doses and multiple doses. In the trials, GEM231 was generally well tolerated. Even in high doses, GEM231 did not show some of the side effects normally associated with most current cancer treatments or with 1st generation antisense compounds.

GEM92 for the Treatment of HIV-1. GEM92 is a 2nd generation antisense compound that is targeted to the specific region of the human immunodeficiency virus HIV-1. Based on the clinical experience we gained with GEM91, our 1st generation antisense compound that also targeted the same region of HIV-1, we created chemical modifications to improve the side effects profile and to enhance the stability of the compound. In 1997, we conducted a phase 1 study in the United Kingdom to investigate the safety and pharmacokinetics of single doses of GEM92, given at three different dose levels by the oral route and one does level as a 2-hour intravenous infusion. All doses given in the study were well tolerated by the patients. Further, GEM92 was detected in the blood after both oral dosing and injection, suggesting that GEM92 could be developed as an oral drug. We believe both GEM92's medicinal approach and genetic target are unique in that no antisense drug has been approved for the treatment of AIDS, and no other drug has the same target on the HIV-1 genome. We are not presently moving the development of GEM92 forward due to the success of the currently available combination drug therapies in controlling HIV. However, we continue to monitor trends in HIV treatment and may recommence our development efforts for GEM92, either alone or with a partner, if viral resistance to existing therapies results in the need for a new approach to HIV treatment.

Preclinical Development

We have a number of antisense compounds in the preclinical testing phase of development. The two principal antisense compounds which we have in preclinical development are:

- GEM220, a 2nd generation antisense compound directed against Vascular Endothelial Growth Factor or VEGF. VEGF is a growth factor that contributes to the growth of new blood vessels, which is a process called angiogenesis. In diseases such as cancer, the growth of new blood vessels is critical to the growth of tumors. Because GEM220 is designed to inhibit VEGF, we believe GEM220 can inhibit angiogenesis in malignant tumors and in other disease states such as macular degeneration and psoriasis.

- GEM240, a 2nd generation antisense compound designed to inhibit mdm2. Mdm2 is a protein found in increased levels in many human cancers. Mdm2 binds to tumor suppressor protein p53, which results in reduced suppression of tumor cells by p53 and thereby contributes to the growth of cancer cells. In animal studies, GEM240 has been shown to decrease levels of mdm2 in many types of cancer cells, including colon cancer cells, breast cancer cells and brain cancer cells, and in turn to stabilize p53 levels in these cells.

Cancer Therapy Potentiation

Despite the number of advances that have been made in the treatment of human cancers, currently marketed anticancer therapies often fail to produce sustained antitumor benefits to a cancer patient. In addition, standard therapies available to treat malignancies, such as drugs that work due to their toxicity to cells, and other damaging treatments, like radiation, often produce substantial toxic side effects. Most cancer drugs when used alone have rarely produced sustained antitumor benefits. To address these problems, oncologists have increasingly employed treatment regimens that include a combination of therapies, each of which has demonstrated activity against human malignancies. While this approach has produced improved treatment responses, the side effects of combined treatments are often greater when multiples of toxic drugs are given.

As part of our efforts to develop antisense drugs which could be used as part of cancer combination therapies, we discovered that the combination of oligonucleotide compounds with some prodrug anticancer therapies could enhance or potentiate the antitumor activity of the prodrug included in the combination. Prodrugs are therapies metabolized by the body after administration to produce their most active forms.

We are focusing a significant portion of our efforts on the combination of an antisense oligonucleotide with Camptosar. Camptosar is a prodrug that is altered primarily in the liver to generate an active product designated as SN38. SN38 is considered to be the molecule responsible for most of the antitumor activity of Camptosar. SN38 is also implicated in production of the major side effects encountered clinically with Camptosar. When we tested Camptosar in animals in combination with several different oligonucleotides, we noted both incremental non-antisense and antisense specific tumor activity. In addition, in over ten animal tumor models, the co-administration of GEM231 with Camptosar resulted in enhanced and prolonged suppression of tumor growth in comparison with Camptosar alone.

As part of our ongoing phase 1/2 clinical trials of GEM231 described above, we are studying the changes in the pharmacokinetics of Camptosar when administered in combination with GEM231 because changes in pharmacokinetics may be an indicator of potentiation of Camptosar by GEM231 in patients with solid tumors.

Cyclicons

With the advent of the human genome project, researchers have identified thousands of genes whose functions have not yet been established. In order to design drugs targeting these genes, it is important to understand the role of each gene in normal and disease conditions. We have a program in which our synthetic DNA can be used to determine if a specific gene is a good target for drugs. Our synthetic DNA, designed as antisense molecules, is especially useful in these studies because of its ability to interact with very specific targets.

We have developed a novel circular-structured oligonucleotide, which we refer to as a Cyclicon, for use in drug target validation, drug discovery and as a probe and primer in PCR amplification. PCR amplification is an important process that is widely used in academic laboratories and the biopharmaceutical industry to produce many DNA copies from a single strand of DNA. We have designed our Cyclicons so that when the circular-structured oligonucleotide binds to messenger RNA, the circular structure of the oligonucleotide is disrupted and fluorescence is emitted. As a result, drug developers can use our Cyclicons as a tool to measure when and where reactions between an antisense sequence and messenger RNA occur.

Research and Development

For the years ended December 31, 2002, 2001 and 2000, we spent approximately $7.9 million, $4.9 million and $3.6 million, respectively, on research and development activities. Third parties sponsored only a nominal portion of these research and development activities in 2002, 2001 and 2000.

Patents, Proprietary Rights and Licenses

Patents and Proprietary Rights

Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

As of February 28, 2003, we owned or exclusively licensed 91 issued U.S. patents and 79 U.S. patent applications and 143 corresponding foreign patents and over 184 corresponding foreign patent applications. The issued patents held or exclusively licensed by us include composition of matter patents on our own advanced DNA chemistries covering the use of these chemistries with various genes or sequences, patents

covering therapeutic targets, patents covering immune modulation and patents covering oral and other routes of administering our synthetic DNA. These issued patents expire at various dates ranging from 2006 to 2023.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. Our ability to maintain and solidify our proprietary position for our technology will depend on our success in obtaining effective claims and enforcing those claims once granted. We do not know whether any of our patent applications or those patent applications which we license will result in the issuance of any patents. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, invalidated or circumvented, and the rights granted thereunder may not provide us proprietary protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies or duplicate any technology developed by us. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our products can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thus reducing any advantage of the patent, which could adversely affect our ability to protect future drug development and, consequently, our operating results and financial position.

Because patent applications in the United States and many foreign jurisdictions are typically not published until eighteen months after filing and because publications of discoveries in the scientific literature often lag behind actual discoveries, we cannot be certain that we were the first to make the inventions claimed in each of our issued patents or pending patent applications, or that we were the first to file for protection of the inventions set forth in these patent applications.

Litigation may be necessary to defend against or assert claims of infringement, to enforce patents issued to us, to protect trade secrets or know-how owned by us, or to determine the scope and validity of the proprietary rights of others. In addition, interference proceedings declared by the U.S. Patent and Trademark Office may be necessary to determine the priority of inventions with respect to our patent applications. Litigation or interference proceedings could result in substantial costs to and diversion of effort by us, and could have a material adverse effect on our business, financial condition and results of operations. These efforts by us may not be successful.

Trade Secrets

We may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets are difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants, scientific advisors and other contractors. There can be no assurance that these agreements will not be breached, that we will have adequate remedies for any breach, or that our trade secrets will not otherwise become known or be independently discovered by competitors. To the extent that our employees, consultants or contractors use intellectual property owned by others in their work for us, disputes may also arise as to the rights in related or resulting know-how and inventions.

Licenses

We are a party to a number of royalty-bearing license agreements under which we have acquired rights to patents, patent applications and technology of third parties. Our principal license agreement is with University of Massachusetts Medical Center. Under the terms of our license agreement with UMass Medical Center, we are the worldwide, exclusive licensee under a number of U.S. issued patents and various patent applications owned by UMass Medical Center relating to antisense oligonucleotides and their production and use. Many of these patents and patent applications have corresponding applications on file or corresponding patents in other major industrial countries.

Seventeen of the issued U.S. patents and 28 of the issued foreign patents licensed by us from the University of Massachusetts Medical Center broadly claim the use of our hybrid antisense oligonucleotides and ribozymes. The other issued U.S. patents covered by the license agreement include claims covering composition and uses of oligonucleotides based on advanced chemistries, and compositions of certain modified oligonucleotides that are useful for diagnostic tests or assays. The patents licensed to us by the University of

Massachusetts Medical Center expire at dates ranging from 2006 to 2019. This license expires upon the expiration of the last to expire of the patents covered by the license.

Other license agreements under which we are the licensee include:

- an exclusive license agreement with McGill University covering patent applications relating to synthetic DNA and DNA Methyltransferase,
- an exclusive license agreement with Massachusetts General Hospital covering patents and patent applications jointly owned by us and Massachusetts General Hospital directed to compositions and use of antisense applied to Alzheimer's disease,
- an exclusive license agreement with Louisiana State University covering patents and patent applications jointly owned by us and Louisiana State University relating to MDM2,
- a non-exclusive license agreement with Genzyme Corporation covering patents and patent applications relating to MDM2,
- a non-exclusive license agreement with Integrated DNA Technologies, Inc., covering patents and patent applications that broadly claim chemical modifications to synthetic DNA, and
- an exclusive license agreement with Dr. Yoon S. Cho-Chung covering patents and patent applications relating to Protein Kinase A.

Under these licenses we are obligated to pay royalties on net sales by us of products or processes covered by a valid claim of a patent or patent application licensed to us. We also are required in some cases to pay a specified percentage of any sublicense income that we may receive. These licenses impose various commercialization, sublicensing, insurance and other obligations on us. Our failure to comply with these requirements could result in termination of the licenses. Each of these licenses terminates upon the expiration of the last to expire of the patents covered by the license.

Corporate Alliances

An important part of our business strategy is to enter into research and development collaborations, licensing agreements and other strategic alliances, primarily with biotechnology and pharmaceutical corporations, to develop and commercialize drugs based on our technologies.

Isis Pharmaceuticals, Inc.

In May 2001, we entered into a collaboration and license agreement with Isis. Under the agreement, we granted Isis a license, with the right to sublicense, to our antisense chemistry and delivery patents and patent applications. We retained the right to use these patents and patent applications in our own drug discovery and development efforts and in collaborations with third parties. In consideration of the license, Isis agreed to pay us $15.0 million in cash plus shares of Isis common stock in four installments intended to have an aggregate value of $19.5 million based on the stock price of the Isis common stock on the dates of issuance of the shares. In 2001, Isis paid $15.0 million to us in cash and issued to us as the first three installments of its equity payment obligation 857,143 shares of its common stock having an aggregate fair market value on the dates on which title to the shares was received of $17.3 million. The remaining $4.5 million installment was scheduled to be paid in 2003. Under the agreement, Isis is also required to pay us a portion of specified sublicense income it receives from some types of sublicenses of our patents and patent applications. In February 2003, Isis made such a payment to us in connection with two sublicenses of our patents and patent applications.

In addition under the agreement, we licensed from Isis specified antisense patents and patent applications, principally Isis' suite of RNase H patents and patent applications. We have the right under the agreement to use these patents and patent applications in our drug discovery and development efforts and in some types of collaborations with third parties. In consideration of this license, we agreed to pay Isis a total of $6.0 million in cash or in shares of our common stock in three equal annual installments of $2.0 million beginning in May 2002. We also agreed to pay Isis a nominal annual maintenance fee and a modest royalty on

sales of products covered by specified patents and patent applications sublicensed to us by Isis. In May 2002, we made our first installment payment to Isis consisting of approximately $716,000 in cash and 1,005,499 shares of our common stock having a fair market value of approximately $1.2 million on the date of issuance.

In August 2002, we amended our collaboration and license agreement with Isis. The amendment limited each party's obligation to participate in collaboration committee meetings and terminated the obligations of each party to pay the remaining installment payments due from each party under the agreement. The amendment did not affect our retained rights to use the patents and patent applications we licensed to Isis in the original agreement or our rights to the patents and patent applications which we licensed from Isis.

The licenses granted under the Isis agreement terminate upon the last to expire of the patents and patent applications licensed under the agreement. We may terminate at any time the sublicense by Isis to us of the patents and patent applications for which we have maintenance fee and royalty obligations to Isis.

MethylGene Inc.

In 1996, we and three Canadian institutional investors formed MethylGene Inc. In connection with the formation of MethylGene, we made a cash investment in MethylGene and granted to MethylGene an exclusive, royalty-free worldwide license to antisense patents, patent applications and technology owned or exclusively licensed by us from University of Massachusetts Medical Center and McGill University to develop and market the following:

- antisense compounds which inhibit the production of DNA methyltransferase for any indication;
- other methods of inhibiting DNA methyltransferase for any indication; and
- antisense compounds to inhibit up to two additional molecular targets for any indication.

In consideration for the cash investment and the license, we received shares of capital of MethylGene. In 2001, we sold all of our shares in MethylGene to an institutional investor and a group of Canadian institutional investors for an aggregate purchase price of $7.2 million.

Other Antisense Collaborations

We are a party to three collaboration and license arrangements involving the use of our antisense technologies and specified indications.

- *Aegera Therapeutics Inc.* We are a party to an agreement with Aegera which relates to the development of an antisense drug targeted to the XIAP gene, a gene which has been implicated in the resistance of cancer cells to chemotherapy.
- *Epigenesis Pharmaceuticals, Inc.* We are a party to an agreement with Epigenesis which relates to the development of up to five antisense drugs for the treatment of respiratory disease.
- *Micrologix Biotech Inc.* We are a party to an agreement with Micrologix which relates to the development of an antisense drug for the treatment of human papillomavirus. Origenix, a former subsidiary of ours, and the entity from which Micrologix acquired the rights to the development, previously conducted a phase 1 clinical trial of this drug candidate.

Under these arrangements, we typically license to our collaborative partner our antisense chemistry and delivery patents and patent applications on a non-exclusive basis, and any antisense patents and patent applications that we have that are directed at the genes that are the subject of the arrangement on an exclusive basis. In addition, although our collaborative partners are responsible for the development and commercialization of the product, we typically provide specified research, development and compound optimization services to our collaborative partner. In consideration for the license and these services, we typically receive license fees and are entitled to receive research payments, payments upon achievement of development milestones and royalties on product sales and sublicensing, if earned. The licenses granted under these agreements typically terminate upon the later of the last to expire of the patents licensed under the agreements or a specified number of years after the first commercial sale of products covered by the agreements. These

agreements may be terminated by either party upon a material breach. Our collaborative partners may terminate these agreements at any time upon written notice.

Academic and Research Collaborations

We have entered into a number of collaborative research relationships with independent researchers, leading academic and research institutions and U.S. government agencies. These research relationships allow us to augment our internal research capabilities and obtain access to specialized knowledge and expertise.

In general, our collaborative research agreements require us to pay various amounts to support the research. We usually provide the synthetic DNA for the collaboration, which the collaborator then tests. If in the course of conducting research under its agreement with us a collaborator, solely or jointly with us, creates any invention, we generally have an option to negotiate an exclusive, worldwide, royalty-bearing license to the invention. Inventions developed solely by our scientists in connection with a collaborative relationship generally are owned exclusively by us. Most of these collaborative agreements are nonexclusive and can be cancelled with limited notice.

Government Regulation

The testing, manufacturing, labeling, advertising, promotion, export, and marketing, among other things, of drugs are extensively regulated by governmental authorities in the U.S. and other countries. In the U.S., the FDA regulates pharmaceutical products under the Federal Food, Drug, and Cosmetic Act, or FDCA, and other laws. Both before and after approval is obtained, violations of regulatory requirements may result in various adverse consequences, including the FDA's delay in approving or refusal to approve a drug, suspension or withdrawal of an approved product from the market, operating restrictions, and the imposition of civil or criminal penalties.

The steps required before a product may be approved for marketing in the U.S. generally include:

- preclinical laboratory tests and animal tests,
- the submission to the FDA of an investigational new drug application, or IND, for human clinical testing, which must become effective before human clinical trials may begin,
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the product, and
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is made to assess compliance with the FDA's good manufacturing practices regulations, or GMP.

Preclinical tests include laboratory evaluation of the product, as well as animal studies to assess the potential safety and efficacy of a drug. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND, which must become effective before human clinical trials may be commenced. The IND will automatically become effective 30 days after its receipt by the FDA, unless the FDA before that time raises concerns or questions about the conduct of the trials as outlined in the IND. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed. We cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined, and certain phases may be eliminated.

- In phase 1, the initial introduction of the drug into human subjects, the drug is usually tested for safety or adverse effects, dosage tolerance, and pharmacologic action;
- Phase 2 usually involves studies in a limited patient population to:
  - evaluate preliminarily the efficacy of the drug for specific, targeted conditions,

- determine dosage tolerance and appropriate dosage, and
- identify possible adverse effects and safety risks; and

- Phase 3 trials generally further evaluate clinical efficacy and test further for safety within an expanded patient population.

We, or the FDA, may suspend clinical trials at any time on various grounds, including a finding that the patients are being exposed to an unacceptable health risk.

The results of the preclinical and clinical studies, together with other detailed information, including information on the manufacture and composition of the product, are submitted to the FDA as part of a new drug application for approval prior to the marketing and commercial shipment of the product. The FDA may deny a new drug application if all applicable regulatory criteria are not satisfied or may require additional clinical, toxicology or manufacturing data. Even after a new drug application results in approval to market a product, the FDA may withdraw product approval if compliance with regulatory standards is not maintained or if safety problems occur after the product reaches the market. In addition, the FDA requires surveillance programs to monitor the consistency of manufacturing and the safety of approved products that have been commercialized. The agency has the power to require changes in labeling or to prevent further marketing of a product based on new data that may arise after commercialization. Also, new federal, state, or local government requirements may be established that could delay or prevent regulatory approval of our products under development.

We will also be subject to a variety of foreign regulations governing clinical trials and sales of our products. Whether or not FDA approval has been obtained, approval of a product by the comparable regulatory authorities of foreign countries must be obtained prior to the commencement of marketing of the product in those countries. The approval process varies from country to country and the time may be longer or shorter than that required for FDA approval. For marketing outside the U.S., we are also subject to foreign regulatory requirements governing human clinical trials and marketing approval for products. The requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary greatly from country to country.

In addition to regulations enforced by the FDA, we are also subject to regulation under the Occupational Safety and Health Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act, and other present and potential future federal, state, or local regulations. Our research and development activities involve the controlled use of hazardous materials, chemicals and various radioactive compounds. Although we believe that our safety procedures for handling and disposing of such materials comply with the standards prescribed by state and federal regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of such an accident, we could be held liable for any damages that result and any such liability could exceed our resources.

Manufacturing

We are party to a supply agreement with Avecia Biotechnology under which we purchase our requirements for oligonucleotide compounds from Avecia at a preferential price. We are purchasing all of the oligonucleotides we are using in our ongoing clinical trials and pre-clinical testing from Avecia under this agreement. This agreement expires in March 2004. We expect that we will seek to enter into a longer term arrangement with Avecia or new arrangements with third-party manufacturers to supply us with the oligonucleotide compounds that we need for our research, preclinical, clinical and commercial supply purposes.

Competition

We expect that our product candidates will address several different markets defined by the potential indications for which these product candidates are developed and ultimately approved by regulatory authorities. For several of these indications, these product candidates will be competing with products and therapies either currently existing or expected to be developed, including IMO compounds and antisense oligonucleotides developed by third parties.

Competition among these products and therapies will be based, among other things, on

- product efficacy,
- safety,
- reliability,
- availability,
- price, and
- patent position.

The timing of market introduction of our products and competitive products will also affect competition among products. We also expect the relative speed with which we can develop products, complete the clinical trials and approval processes and supply commercial quantities of the products to the market to be an important competitive factor. Our competitive position will also depend upon our ability to attract and retain qualified personnel, to obtain patent protection or otherwise develop proprietary products or processes and to secure sufficient capital resources for the often substantial period between technological conception and commercial sales.

There are a number of companies, both privately and publicly held, that are conducting research and development, preclinical and clinical and commercial activities relating to technologies and products that are similar to our technologies and products, including large pharmaceutical companies with programs in IMO-like compounds or antisense technology and biotechnology companies with similar programs. Our principal competitors include Isis, Genta Incorporated, Coley Pharmaceutical Group and Dynavax Technologies Corp.

The primary indications for which we are developing our antisense and IMO products are cancer and infectious diseases. None of our competitors are currently marketing any antisense or IMO-like products for cancer or infectious diseases, except for Isis which is currently marketing an antisense product for the treatment of cytomegalovirus retinitis in patients with AIDS. However, our competitors are developing a number of product candidates for cancer and infectious diseases that are currently in clinical trials. In particular,

- Isis has six compounds presently in clinical trials, one of which is in late-stage clinical trials. Of these compounds, four are being studied for the treatment of cancer or infectious diseases.
- Genta has one compound in late-stage clinical trials being studied for the treatment of cancer.
- Dynavax has an IMO-like compound in clinical trials for four indications. These indications include the treatment of cancer and infectious disease.
- Coley has an IMO-like compound in clinical trials for three indications. These indications include treatment of cancer and infectious disease.

Many of our competitors, particularly the pharmaceutical and large biotechnology companies with which we compete, have substantially greater financial, technical and human resources than we have. In addition, many of our competitors have significantly greater experience than we have in undertaking preclinical studies and human clinical trials of new pharmaceutical products, obtaining FDA and other regulatory approvals of products for use in health care and manufacturing, marketing and selling approved products.

Employees

As of February 28, 2003, we employed 27 individuals full-time, including 20 employees in research and development. Seventeen of our employees have an M.D. and/or a Ph.D. None of our employees are covered by a collective bargaining agreement, and we consider relations with our employees to be good.

Item 2. ***Properties***

We lease approximately 26,000 square feet of laboratory and office space, including 6,000 square feet of specialized preclinical lab space, in Cambridge, Massachusetts under a lease that expires April 30, 2007. We believe these facilities are adequate to accommodate our needs for the near term.

Item 3. ***Legal Proceedings***

We are not a party to material legal proceedings.

Item 4. ***Submission of Matters to a Vote of Security Holders***

No matters were submitted to a vote of security holders in the quarter ended December 31, 2002.

Executive Officers and Key Employees of Hybridon

The following table sets forth the names, ages and positions of our executive officers and other key employees as of February 28, 2003:

Name	Age	Position
Stephen R. Seiler	46	Chief Executive Officer and Director
Sudhir Agrawal, D. Phil	49	President, Chief Scientific Officer and Director
Robert G. Andersen	52	Chief Financial Officer, Vice President of Operations, Treasurer and Secretary
R. Russell Martin, M.D.	67	Senior Vice President of Drug Development
Jinyan Tang, Ph.D.	59	Vice President of Chemistry

Stephen R. Seiler was appointed our Chief Executive Officer and elected to our board of directors on September 1, 2001. Prior to joining us, Mr. Seiler served as Executive Vice President, Planning Investment & Development at Elan Corporation plc from 1995 to 2001. While at Elan, Mr. Seiler took part in and oversaw activities in a wide range of areas including acquisitions, divestitures and in and out licensing. From 1991 to 1995, Mr. Seiler worked as an Investment Banker at Paribas Capital Markets in both London and New York. He was founder and head of Paribas's pharmaceutical industry investment banking group. In that capacity, he initiated and worked on a wide variety of transactions including initial public offerings, privatizations, mergers and acquisitions debt and equity offerings and derivative transactions. Mr. Seiler received a J. D. from Georgetown University with Honors in 1980 and a B.A. summa cum laude in History from the University of Notre Dame in 1977. He is a member of the Board of Associates of the Whitehead Institute. He is also a member of the bar in New York, Arizona, and Missouri.

Dr. Sudhir Agrawal joined us in 1990 and has served as our Chief Scientific Officer since January 1993, our Senior Vice President of Discovery since March 1994, our President since February 2000 and as a director since March 1993. Prior to his appointment as Chief Scientific Officer, he served as our Principal Research Scientist from February 1990 to January 1993 and as our Vice President of Discovery from December 1991 to January 1993. He served as Acting Chief Executive Officer from February 2000 until September 2001. Prior to joining us, Dr. Agrawal served as a Foundation Scholar at the Worcester Foundation from 1987 through 1991. Dr. Agrawal served as a Research Associate at the Medical Research Council's Laboratory of Molecular Biology in Cambridge, England from 1985 to 1986, studying DNA chemistry and synthetic oligonucleotides. Dr. Agrawal received a D. Phil in chemistry in 1980, an M.Sc in organic chemistry in 1975 and a B.Sc. in chemistry, botany and zoology in 1973 from Allahaban University in India. Dr. Agrawal is one of the most published researchers in the field of antisense technology. He has authored more than 200 research papers and reviews and has edited three books. He is a member of the editorial board of Antisense Research & Development Journal, Trends in Molecular Medicine, Investigational Drug Journal, and Current Cancer Drug Targets, and is associate editor of Molecular Biotechnology.

Robert G. Andersen joined us in November 1996 as Vice President of Systems Engineering and Management Information Systems and has served as our Vice President of Operations since 1997, our Treasurer since March 1998 and our Chief Financial Officer since February 2000. Prior to joining us,

Mr. Andersen served in a variety of management positions at Digital Equipment Corporation from 1986 to 1996, most recently as Group Manager of the Applied Objects Business Unit. From 1978 to 1986, Mr. Andersen held technical management positions at United Technologies Corporation, most recently as Director of Quality for Otis Elevator Company's European Operations based in Paris, France and Worldwide Director of Controls for Otis Group. Mr. Andersen received an M.S. in Management from Northeastern University in 1978 and his B.E.E. magna cum laude in Electrical Engineering from The City College of New York in 1972. He is also a graduate of the United Technologies Advanced Studies Program.

Dr. R. Russell Martin joined us in 1994 and has served as our Senior Vice President of Drug Development since 1998. He served as our Vice President of Drug Development from 1996 through 1998 and our Vice President of Clinical Research from 1994 through 1996. Prior to joining us, Dr. Martin served in a variety of positions at Bristol-Myers Squibb from 1983 to 1993, most recently as Vice President of Infectious Diseases Clinical Research. Prior to joining the pharmaceutical industry, Dr. Martin was associate professor at Indiana University School of Medicine and Professor of Medicine, Microbiology and Immunology at Baylor College of Medicine from 1971 to 1983. Dr. Martin received a M.D. degree from the Medical College of Georgia in 1960 and an A.B. degree in American Studies from Yale University in 1956. He is a Fellow of the American College of Physicians and of the Infectious Diseases Society of America.

Dr. Jinyan Tang joined us in 1991 and has served as our Vice President of Chemistry since 2000. Dr. Tang was our Vice President of Process Research and Development from 1995 to 1997 and Vice President of Production from 1997 to 2000. Prior to joining us, Dr. Tang served as Visiting Fellow at the Worcester Foundation from 1988 to 1991. Dr. Tang served as Visiting Research Professor at the University of Colorado in 1988 and Associate Professor at the Shanghai Institute of Biochemistry, Chinese Academy of Sciences from 1985 to 1988 where he specialized in oligonucleotide chemistry. Dr. Tang received a B.Sc. in Biochemistry in 1965 and a Ph.D. of Biochemistry in 1978 from the Shanghai Institute of Biochemistry, Chinese Academy of Sciences.

PART II.

Item 5. *Market For Registrant's Common Equity and Related Stockholder Matters*

Market Information

Our common stock is quoted on the OTC Bulletin Board under the symbol "HYBN.OB". Quotes on the OTC Bulletin Board may reflect inter-dealer prices, without retail markups, markdowns or commissions and do not necessarily represent actual transactions.

The following table sets forth, for the periods indicated, the high and low sales prices per share of our common stock during each of the quarters set forth below as reported on the OTC Bulletin Board:

	High	Low
2002		
First Quarter	$1.85	$1.23
Second Quarter	1.49	0.92
Third Quarter	1.23	0.59
Fourth Quarter	1.25	0.62
2001		
First Quarter	$0.72	$0.41
Second Quarter	1.51	0.41
Third Quarter	1.30	0.70
Fourth Quarter	2.01	0.71

The number of common stockholders of record on February 28, 2003 was 320.

We have never declared or paid cash dividends on our common stock and we do not expect to pay any cash dividends on our common stock in the foreseeable future. The indenture under which we issued 9% convertible subordinated notes in April 1997 limits our ability to pay dividends or make other distributions on our common stock or to pay cash dividends on our convertible preferred stock. As of February 28, 2003, 9% notes in the aggregate principal amount of $1.3 million remained outstanding. The 9% notes are due in April 2004.

Our Series A preferred stock pays dividends at 6.5% per year, payable semi-annually in arrears. We may pay these dividends either in cash or in additional shares of Series A preferred stock, at our discretion subject to the restriction under the indenture described above. As of February 28, 2003, we have only paid these dividends in shares of Series A preferred stock.

Sales of Unregistered Securities

Sales by us during the year ended December 31, 2002 of securities that were not registered under the Securities Act of 1933, as amended, included the following:

- During 2002, holders of 3,911 shares of our Series A preferred stock converted such shares into 92,024 shares of our common stock. We relied upon Section 3(a)(9) of the Securities Act of 1933 as an exemption from registration for the newly issued common stock.
- On May 24, 2002, we issued 1,005,499 shares of our common stock as payment to Isis as part of the first installment payment due to Isis under our collaboration and license agreement with Isis. We relied upon Section 4(2) of the Securities Act of 1933 as an exemption from registration for the newly issued common stock.
- In November 2002, holders of our 8% notes in the aggregate principal amount of approximately $32,000 converted the principal and accrued interest thereon into 52,637 shares of our common stock. We relied upon Section 3(a)(9) of the Securities Act of 1933 as an exemption from registration for the newly issued common stock.

- In December 2002, holders of warrants to purchase an aggregate of 1,997,188 shares of our common stock with an exercise price of $0.60 per share, exercised these warrants, pursuant to the cashless exercise provisions of the warrants, for 247,355 shares of our common stock. We relied upon Section 3(a)(9) of the Securities Act of 1933 as an exemption from registration for the newly issued common stock.

Item 6. *Selected Financial Data*

The selected financial data presented below for the year ended December 31, 2002 have been derived from our consolidated financial statements and have been audited by Ernst & Young, LLP, independent auditors. The selected financial data presented below for the years ended December 31, 2001, 2000, 1999 and 1998 have been derived from our consolidated financial statements, as adjusted to reflect the disposition of Hybridon Specialty Products, our oligonucleotide manufacturing division HSP, as discontinued operations, and have been audited by Arthur Andersen LLP, our former independent public accountants. The financial data should be read along with, and are qualified by reference to, "Management's Discussion and Analysis of Financial Condition and Results of Operations," our consolidated financial statements and notes thereto and the Report of Independent Public Accountants included elsewhere in this annual report on Form 10-K.

	Year Ended December 31,				
	2002	2001	2000	1999	1998
	(In thousands, except per share data)				
Statement of Operations Data:					
Revenues:					
License fees	$ 29,550	$ 988	$ 179	$ —	$ —
Research and development	10	—	—	600	1,100
Royalty and other income	46	134	83	123	—
Service revenue	—	—	82	365	375
Investment income	650	577	229	92	148
Total revenues	30,256	1,699	573	1,180	1,623
Operating expenses:					
Research and development	7,877	4,868	3,620	5,783	14,183
General and administrative	7,054	5,051	3,184	3,664	6,573
Stock-based compensation from repriced options	(1,297)	1,762	—	—	—
Interest	150	1,319	2,154	683	2,820
Total operating expenses	13,784	13,000	8,958	10,130	23,576
Gain on sale of securities, net	—	5,217	—	—	—
Income (loss) from continuing operations	16,472	(6,084)	(8,385)	(8,950)	(21,953)
Income (loss) from discontinued operations(2)	—	2,663	5,462	(1,553)	(4,028)
Income (loss) before income taxes and extraordinary item	16,472	(3,421)	(2,923)	(10,503)	(25,981)
Income tax credit (provision)	500	(500)	—	—	—
Income (loss) before extraordinary items	16,972	(3,921)	(2,923)	(10,503)	(25,981)
Extraordinary item:					
Gain on conversion of 9% convertible subordinated notes payable	—	—	—	—	8,877
Loss on conversion of 8% convertible subordinated notes payable	—	(1,412)	—	—	—
Net income (loss)	16,972	(5,333)	(2,923)	(10,503)	(17,104)
Accretion of preferred stock dividend	(4,246)	(8,342)	(4,087)	(4,232)	(2,689)
Net income (loss) applicable to common stockholders	$ 12,726	$ (13,675)	$ (7,010)	$ (14,735)	$ (19,793)
Basic net income (loss) per common share from:					
Continuing operations	$ 0.36	$ (0.21)	$ (0.48)	$ (0.57)	$ (1.85)
Discontinued operations	—	0.09	0.31	(0.10)	(0.34)
Extraordinary (loss) gain	—	(0.05)	—	—	0.75
Net income (loss) per share	0.36	(0.17)	(0.17)	(0.66)	(1.44)
Accretion of preferred stock dividends	(0.09)	(0.27)	(0.23)	(0.27)	(0.23)
Net income (loss) per share applicable to common stockholder	$ 0.27	$ (0.44)	$ (0.40)	$ (0.93)	$ (1.67)
Diluted net income (loss) per common share from:					
Continuing operations	$ 0.32	$ (0.21)	$ (0.48)	$ (0.57)	$ (1.85)
Discontinued operations	—	0.09	0.31	(0.10)	(0.34)
Extraordinary (loss) gain	—	(0.05)	—	—	0.75
Net income (loss) per share	0.32	(0.17)	(0.17)	(0.66)	(1.44)
Accretion of preferred stock dividends	(0.08)	(0.27)	(0.23)	(0.27)	(0.23)
Net income (loss) per share applicable to common stockholders	$ 0.24	$ (0.44)	$ (0.40)	$ (0.93)	$ (1.67)
Shares used in computing basic net income (loss) per common share(1)	46,879	30,820	17,418	15,811	11,859
Shares used in computing diluted net loss per common share(1)	52,984	30,820	17,418	15,811	11,859
Balance Sheet Data:					
Cash, cash equivalents and short-term investments(3)	$ 19,175	$ 31,834	$ 3,532	$ 2,552	$ 5,608
Working capital (deficit)	17,638	27,259	(4,238)	(6,534)	(5,306)
Total assets	21,249	32,309	10,001	10,717	15,092
Restricted cash	—	—	5,000	—	—
Capital lease obligations, current portion	34	—	—	—	—
9% convertible subordinated notes payable	1,306	1,306	1,306	1,306	1,306
8% convertible subordinated notes payable	—	288	8,046	6,100	—
Series A convertible preferred stock	7	6	6	7	6
Accumulated deficit	(261,143)	(273,868)	(260,193)	(253,183)	(238,448)
Total stockholders' equity (deficit)	17,444	(33)	(7,530)	(6,072)	2,249

(1) Computed on the basis described in Note 15 of notes to consolidated financial statements appearing elsewhere in this annual report on Form 10-K.

(2) Consolidated financial statements have been restated to reflect the financial results of HSP as a discontinued operation for the years ended December 31, 2001, 2000, 1999 and 1998. Reported revenues, expenses and cash flows exclude the operating results of the discontinued operations.

(3) Short-term investments consisted of U.S. government and corporate bonds with maturities greater than ninety days but less than one year from the balance sheet date.

Quarterly Operating Results (Unaudited)

The following table presents the unaudited statement of operations data for each of the eight quarters in the period ended December 31, 2002. The information for each of these quarters is unaudited, but has been prepared on the same basis as the audited financial statements appearing elsewhere in this annual report on Form 10-K. In the Company's opinion, all necessary adjustments, consisting only of normal recurring adjustments, have been made to present fairly the unaudited quarterly results when read in conjunction with the audited financial statements and the notes thereto appearing elsewhere in this document. These operating results are not necessarily indicative of the results of operations that may be expected for any future period.

	Three Months Ended							
	Dec. 31 2002	Sep. 30 2002	Jun. 30 2002	Mar. 31 2002	Dec. 31 2001	Sep. 30 2001	Jun. 30 2001	Mar. 31 2001
	(In thousands, except per share data)							
Statement of Operations Data:								
Revenue as reported(2)	$ 160	$26,227	$ 818	$ 828	$ 666	$ 344	$ 388	$ 164
Reclassification(2)	—	2,105	59	59	41	58	39	—
Revenues as revised(2)	160	28,332	877	887	707	402	427	164
Operating expenses:								
Research and development	2,270	2,794	1,567	1,246	1,428	1,080	1,259	1,101
General and administrative as reported(2)	1,219	1,246	1,283	1,083	791	1,523	1,253	1,347
Reclassification(2)	—	2,105	59	59	41	58	39	—
General and administrative as revised(2)	1,219	3,351	1,342	1,142	832	1,581	1,292	1,347
Stock-based compensation from repriced options	(116)	(438)	(480)	(263)	1,415	(577)	924	—
Interest	36	38	38	38	218	515	272	315
Total operating expenses	3,409	5,745	2,467	2,163	3,893	2,599	3,747	2,763
Gain (loss) on sale of securities, net	—	—	—	—	(502)	(1,171)	6,890	—
Income (loss) before provision for income taxes	(3,249)	22,587	(1,590)	(1,276)	(3,688)	(3,368)	3,570	(2,598)
Income tax credit (provision)	—	—	—	500	(100)	—	(400)	—
Income (loss) from continuing operations	(3,249)	22,587	(1,590)	(776)	(3,788)	(3,368)	3,170	(2,598)
Income from discontinued operations	—	—	—	—	695	1,968	—	—
Income (loss) before extraordinary gain	(3,249)	22,587	(1,590)	(776)	(3,093)	(1,400)	3,170	(2,598)
Extraordinary item:								
Loss on conversion of 8% convertible subordinated notes payable	—	—	—	—	—	—	—	(1,412)
Net income (loss)	(3,249)	22,587	(1,590)	(776)	(3,093)	(1,400)	3,170	(4,010)
Accretion of preferred stock dividend	(1,074)	(1,073)	(1,059)	(1,040)	(1,040)	(5,113)	(1,181)	(1,008)
Net income (loss) applicable to common stockholders	$(4,323)	$21,514	$(2,649)	$(1,816)	$(4,133)	$(6,513)	$ 1,989	$(5,018)
Basic net income (loss) per share applicable to common stockholders	$ (0.09)	$ 0.45	$ (0.06)	$ (0.04)	$ (0.09)	$ (0.16)	$ 0.11	$ (0.27)
Diluted net income (loss) per share applicable to common stockholders	$ (0.09)	$ 0.34	$ (0.06)	$ (0.04)	$ (0.09)	$ (0.16)	$ 0.04	$ (0.27)
Shares used in computing income (loss) per common share(1)								
Basic	47,575	47,527	46,708	45,670	45,559	40,211	18,854	18,489
Diluted	47,575	66,950	46,708	45,670	45,559	40,211	57,174	18,489

(1) Computed on the basis described in Note 15 of Notes to consolidated financial statements appearing elsewhere in this annual report on Form 10-K.

(2) In the fourth quarter of 2002 the Company reclassified certain direct and incremental costs related to the May 2001 Isis agreement from Revenues to General and Administrative Expenses.

Item 7. ***Management's Discussion and Analysis of Financial Condition and Results of Operations***

We are a leading company in the discovery and development of novel therapeutics and diagnostics using synthetic DNA. Our activities are based on four technologies:

- Our immunomodulatory oligonucleotide, or IMO, technology uses synthetic DNA that contains specific sequences that mimic bacterial DNA to modulate responses of the immune system.
- Our antisense technology uses synthetic DNA to block the production of disease causing proteins at the cellular level.
- Our cancer therapy potentiation technology uses synthetic DNA to enhance the antitumor activity of certain marketed anticancer drugs and increase their effectiveness.
- Our Cyclicon technology uses novel synthetic DNA structures, which we refer to as Cyclicons, for identifying gene function in drug target validation and drug discovery.

Since we began operations in February 1990, we have been involved primarily in research and development and manufacturing. To date, almost all of our revenues have been from collaborative and license agreements, interest income and manufacturing of synthetic DNA and reagent products by our DNA manufacturing business, known as the Hybridon Specialty Products Division, or HSP, prior to our selling HSP in September 2000.

We have incurred total losses of $261.1 million through December 31, 2002 and expect to incur substantial operating losses in the future. In order to commercialize our therapeutic products, we need to address a number of technological challenges and to comply with comprehensive regulatory requirements. In 2003, we expect that our research and development and general and administrative expenses will be similar to those in 2002, excluding the $2.2 million in general and administrative expenses relating to the amendment to our agreement with Isis, as we use the cash resources that we obtained in 2000 and 2001 to continue our discovery and development programs.

Recent Developments

Stock Repurchase. In February 2003, we repurchased 4,643,034 shares of our common stock at a price of $1.15 per share from two Middle Eastern stockholders and their affiliates. The fair market value of our common stock was $0.75 per share on the date of the transaction resulting in a premium of $1.9 million in the aggregate. We charged this premium to general and administrative expense in the quarter ending March 31, 2003.

HSP Sale. In September 2000, we sold HSP and related intellectual property to Avecia Biotechnology for $15.0 million. We received $12.0 million at the closing of the sale and the remaining $3.0 million in September 2001. Our consolidated financial statements have been restated to reflect the financial results of HSP as a discontinued operation for the year ended December 31, 2000. Reported revenues, expenses and cash flows exclude the operating results of the discontinued operations.

Exchange of 8% Notes. In March 2001, holders of $7.6 million of our 8% notes exchanged their notes for 76,046 shares of our Series B preferred stock. As part of the exchange, the 8% note holders released their security interest in $5.0 million of the proceeds from the sale of HSP, which had been held by them as collateral prior to the exchange. Upon maturity of the 8% Notes on November 30, 2002, holders of $31,582 of the remaining 8% Notes plus accrued interest converted such notes into 52,637 shares of common stock. We paid approximately $284,000 to the holders of the remaining 8% Notes in payment of the outstanding principal and accrued interest thereon.

Sale of MethylGene Shares and Payment of Loan. In April and May 2001, we sold our shareholdings in MethylGene which, at the time, represented 22% of the capital of MethylGene. We received total proceeds of $7.2 million from the sale. We used $3.0 million of the proceeds to reduce a $6.0 million loan from six of our stockholders. In September 2001, we paid off the remaining $3.0 million of this loan. In connection with the payoff of the $6.0 million loan, $0.8 million previously deposited to secure the loan was released.

Collaboration and License Agreement with Isis Pharmaceuticals. In May 2001, we entered into a collaboration and license agreement with Isis. In consideration of the license, Isis agreed to pay us $15.0 million in cash and to issue us shares of Isis common stock in four installments intended to have an aggregate value of $19.5 million based on the stock price of the Isis common stock on the dates of issuance of the shares. In 2001, Isis paid $15.0 million to us in cash and issued to us as the first three installments of its equity payment obligation 857,143 shares of its common stock having an aggregate fair market value on the dates on which title to the shares was received of $17.3 million. The remaining $4.5 million installment was due in 2003. In addition, under the agreement, we licensed from Isis specified antisense patents and patent applications, principally, its suite of RNase H antisense patents and patent applications. In return, we agreed to pay Isis a total of $6.0 million in cash or in shares of our common stock in three equal annual installments intended to have an aggregated value of $6.0 million. In May 2002, we made our first installment payment to Isis consisting of 1,005,499 shares of our common stock having a fair market value of approximately $1.2 million on the date of issuance and cash of approximately $716,000.

In August 2002, we amended our collaboration and license agreement with Isis. The amendment limited each party's obligation to participate in collaboration committee meetings and terminated the obligations of each party to pay the remaining installment payments due from each party under the agreement. As a result of the amendment, in the third quarter of 2002 we recognized revenue and expenses of approximately $27.9 million and $2.1 million, respectively, that we had previously deferred.

In accordance with terms of our license agreement with UMass Medical Center, in 2001 we paid UMass $1.2 million in respect of the consideration we received from Isis in 2001.

2001 Early Exercise Program. In the second half of 2001, we effected an "early exercise" program in which we exchanged shares of our common stock for shares of our Series B preferred stock, outstanding warrants and 8% notes. As part of this program:

- holders of our Series B preferred stock exchanged their shares of Series B preferred stock for 19,564,500 shares of our common stock;
- holders of warrants to purchase our common stock with exercise prices per share ranging between $0.60 and $2.40 exchanged their warrants for 4,669,808 shares of our common stock; and
- holders of 8% notes in the aggregate principal amount of $456,000 exchanged the principal and accrued interest on such notes for 1,140,448 shares of our common stock.

Critical Accounting Policies

This management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. On an ongoing basis, management evaluates its estimates and judgments, including those related to revenue recognition. Management bases its estimates and judgments on historical experience and on various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 2 to our consolidated financial statements, we believe the most critical accounting policy affecting the portrayal of our financial condition is revenue recognition. We recognize revenue in accordance with SEC Staff Accounting Bulletin No. 101, or SAB 101. SAB 101 requires that four basic criteria be met before revenue can be recognized:

- persuasive evidence of an arrangement exists;
- delivery has occurred, services have been rendered or obligations have been satisfied;

- the fee is fixed and determinable; and
- collectibility is reasonably assured.

Determination of the last three criteria are based on management's judgments regarding the fixed nature of the fee charged for services rendered or products delivered and the collectibility of these fees. Should changes in conditions cause management to determine these criteria are not met for any future transactions, revenues recognized for any reporting period could be adversely affected.

During 2001, we received a total of $32.3 million in cash and stock under our collaboration and license agreement with Isis. This amount and future amounts due under this license agreement are non-refundable. Prior to amending the agreement in August 2002, we were recognizing the revenue from Isis on a straight-line basis over the 10-year term of the agreement. Our decision to recognize Isis revenue over the term of the Isis agreement was based primarily on a continuing obligation contained in the license agreement which we had interpreted as neither inconsequential nor perfunctory according to SAB 101. In 2002, Isis and we amended the agreement. The amendment limited each party's obligation to participate in collaboration committee meetings and terminated the obligations of each party to pay the remaining installment payments due from each party under the agreement. Based on this amendment, we determined that our obligations under the agreement were inconsequential and perfunctory according to SAB 101 and as such did not preclude recognition of revenue. For this reason, in the third quarter of 2002, we recognized the revenue and directly related and incremental expenses that we had previously deferred.

Results of Operations

Years ended December 31, 2002, 2001 and 2000

Revenues

Total revenues increased by $28.6 million from $1.7 million in 2001 to $30.3 million in 2002. The increase was primarily due to our recognition in the third quarter of 2002 of $27.9 million of deferred revenue as a result of the August 2002 amendment to the license agreement with Isis.

Total revenues increased by $1.1 million from $0.6 million in 2000 to $1.7 million in 2001. The increase was primarily due to license revenues from the agreements entered into in 2001 with Isis and EpiGenesis. In connection with the Isis agreement, we recorded $0.9 million in revenues. The service revenue in 2000 resulted from services performed by us under a license agreement with MethylGene, which terminated in that year. The increase in total revenues in 2001 also reflected increased interest income from higher cash balances as a result of payments from Isis and EpiGenesis, the sale of our interest in MethylGene and the sale of HSP.

Research and Development Expenses

Research and development expenses increased by $3.0 million, or 62%, from $4.9 million in 2001 to $7.9 million in 2002 and by $1.3 million, or 36%, from $3.6 million in 2000 to $4.9 million in 2001. The increase in 2002 from 2001 was primarily attributable to advancement of our drug development program in 2002, including the commencement of clinical trials of GEM231 and the expansion of pre-clinical activity related to our IMO technology, and additional payroll costs resulting from the hiring of seven new employees in 2002 for our scientific discovery and development teams and reflecting the full-year costs of new employees hired in 2001. The increase in 2001 from 2000 was primarily attributable to higher payroll costs associated with, among other things, additional personnel hired as we expanded our discovery efforts and higher patent prosecution costs. In 2001 and 2000, our research and development expenses related primarily to the development of our IMO technology. We expect our research and development expenses in 2003 to remain at approximately the same level as in 2002 as we increase spending on clinical trials in 2003, but reduce our preclinical development efforts.

Our two primary research and development projects relate to:

- HYB2055 is the lead product candidate in our IMO program. In 2002, we incurred approximately $1.8 million in direct expenses in connection with developing HYB2055. These direct expenses included costs of payments to independent contractors and vendors for preclinical studies, drug manufacturing and related costs and patent preparation costs and related filing fees and exclude internal costs such as payroll and overhead. The IND, we submitted to the FDA covering HYB2055 became effective on March 6, 2003. In March 2003, we commenced a phase 1 trial of HYB2055 in the United Kingdom in healthy volunteers. We anticipate commencing a phase 1 trial of HYB2055 in the United States in cancer patients during the second quarter of 2003.

- GEM 231 is a 2nd generation antisense compound for the treatment of cancer. In 2002, we incurred approximately $1.2 million in direct expenses in connection with developing GEM231. These direct expenses included costs of payments to independent contractors and vendors for clinical studies, patent preparation costs and related filing fees and drug manufacturing and related costs and exclude internal costs such as payroll and overhead. We are currently conducting a phase 1/2 clinical trial of GEM231 as a combination therapy with Camptosar. We plan to commence a phase 2 trial using this drug combination in the second half of 2003 based upon pharmacokinetic analysis and other data obtained from the ongoing phase 1/2 trial. Although we participated in several clinical trials of GEM 231 in 2001, the trials were hospital sponsored and the costs for these trials were primarily borne by third parties whose drugs were being tested in the trials in combination with GEM231.

Because these projects are in early stage of development and given the technological and regulatory hurdles likely to be encountered in the development and commercialization of our products, the future timing and costs of our various research and development programs are uncertain.

General and Administrative Expenses

General and administrative expenses increased $2.0 million, or 40%, from $5.1 million to $7.1 million in 2002 compared to 2001 and increased $1.9 million, or 59%, from $3.2 million to $5.1 million in 2001 compared to 2000. The increase in 2002 was primarily due to the recognition of $2.1 million of deferred expenses as a result of the August, 2002 amendment to the license agreement with Isis. The increase in 2001 was primarily due to increased professional fees associated with our Early Exchange Program and the licensing transactions entered into in 2001 and increased payroll expenses resulting from executive compensation awards and two additional employees in general and administrative positions.

Stock-Based Compensation

As a result of our repricing of stock options in September 1999, some of our outstanding stock options are subject to variable plan accounting which requires us to remeasure the intrinsic value of the repriced options through the earlier of the date of exercise, cancellation or expiration at each reporting date. We recorded a credit to operating results of approximately $1.3 million for the year ended December 31, 2002 as a result of a decrease in the intrinsic value of these options. For the year ended December 31, 2001, we incurred a stock-based compensation expense of $1.8 million which resulted from an increase in the intrinsic value of these options. We did not have a stock-based compensation charge prior to 2001 because the fair market value of our common stock at December 31, 2000 was below the exercise price of the repriced options. We expect that compensation charges and credits may occur in the future based upon changes in the intrinsic value of our repriced options.

Interest Expense

Interest expense decreased by $1.1 million from $1.3 million in 2001 to $0.2 million in 2002 and decreased by $0.9 million from $2.2 million in 2000 to $1.3 million in 2001. The decreases in both periods

were primarily attributable to the conversion of $7.6 million of our 8% notes into Series B preferred stock in March 2001 and the repayment of a $6.0 million note payable, which was paid during the second and third quarters of 2001, to six stockholders.

Gain on Sale of Securities

In May 2001, we received $7.2 million from the sale of our MethylGene shares and recorded a related gain of $6.9 million, which was net of $0.3 million in direct transaction costs. This amount was offset by a realized loss of $1.4 million attributable to a loss in the value of the shares of Isis common stock received under our agreement with Isis following the dates of issuance of the shares to us and a loss of $0.3 million relating to direct expenses associated with the Isis agreement.

Income (Loss) from Discontinued Operations

We recognized income from discontinued operations of $2.7 million and $5.5 million for 2001 and 2000, respectively. The 2001 income primarily reflects the receipt of the $3.0 million contingent payment from Avecia under the terms of the HSP sales agreement. The 2000 income includes gain on the sale of HSP of $6.3 million and operating losses of $0.8 million.

Income Tax Credit (Expense)

In 2002, we recognized a $0.5 million tax credit to operations which was a reversal of the income tax expense recorded in 2001 as a result of income subject to the Alternative Minimum Tax or AMT. In March 2002, the National Economic Stabilization and Recovery Act temporarily rescinded the AMT as it applies to us. As a result, we received a $450,000 refund and recognized a $0.5 million credit to operations during 2002. During 2000, we did not have any income subject to the AMT.

Extraordinary Loss

We had an extraordinary loss of $1.4 million in 2001 resulting from the exchange of our Series B preferred stock for 8% notes.

Preferred Stock Dividends

We pay dividends on our Series A preferred stock at a rate of 6.5% per annum. Between March 2001, the date the Series B preferred stock was issued, and July 2001, when all of the Series B preferred stock was exchanged for our common stock, we paid dividends in the form of additional shares of Series B preferred stock at a rate of 8.0% per annum. Accretion of preferred stock dividends was $4.2 million in 2002, $8.3 million in 2001 and $4.1 million in 2000. The increase from 2000 to 2001 and subsequent decrease from 2001 to 2002 reflects a $4.1 million charge to retained earnings related to the exchange of our Series B preferred stock for our common stock as part of our Early Exchange Program in 2001. The charge is equal to the fair value of the common stock issued less the fair value of common stock that would have been issued pursuant to the original conversion terms of the Series B preferred stock.

Net Operating Loss Carryforwards

As of December 31, 2002, we had approximately $224.0 million and $4.2 million of net operating loss and tax credit carryforwards, respectively. The Tax Reform Act of 1986 contains provisions that may limit our ability to utilize net operating loss and tax credit carryforwards in any given year if certain events occur, including cumulative changes in ownership interests in excess of 50% over a three-year period. We have completed several financings since the effective date of the Tax Act, which, as of December 31, 2002, have resulted in ownership changes, as defined under the Tax Act, which will limit our ability to utilize a portion of our available net operating loss carryforwards.

Liquidity and Capital Resources

We require cash to fund our operating expenses, to make capital expenditures and to pay debt service. Historically, we have funded our cash requirements primarily through the following:

- equity and debt financing;
- manufacturing of synthetic DNA and reagent products by HSP prior to its sale in 2000;
- the sale of HSP for which we received a total of $15.0 million in 2000 and 2001;
- license fees and research funding under collaborative and license agreements;
- interest income;
- lease financings; and
- the sale of our shareholding in MethylGene Inc. for which we received a net of $6.9 million in 2001.

Cash Resources and Cash Flows

We had available cash, cash equivalents and investments of $20.1 million at December 31, 2002, a decrease of $11.7 million, from December 31, 2001. This amount includes the approximately $5.3 million in cash we subsequently used to repurchase 4,643,034 shares of our common stock in February 2003. We used approximately $11.0 million of cash for operating activities in 2002. Our principal uses of cash in 2002 were for conducting preclinical studies of our lead preclinical IMO compound, HYB2055, in preparation for the filing of an IND in the first quarter of 2003. We also used our cash to fund our phase 1/2 clinical trials of GEM231.

We believe that, based on our current operating plan, our existing cash resources, after reflecting the use of funds in February 2003 to effect the stock repurchase described above, will be sufficient to fund our cash requirements at least through the end of 2003. Our actual cash requirements will depend on many factors, including particularly the scope and pace of our research and development efforts and our success in entering into strategic alliances.

We do not expect to generate significant additional funds internally until we successfully complete development and obtain marketing approval for products, either alone or in collaboration with third parties, which we expect will take many years. In 2003, we expect to seek additional funds from collaborations with other biotechnology companies or pharmaceutical companies and from additional debt, equity and lease financings. We believe that the key factors that will affect our internal and external sources of cash are:

- the success of our clinical and preclinical development programs;
- the receptivity of the capital markets to financings by biotechnology companies; and
- our ability to enter into strategic collaborations with biotechnology and pharmaceutical companies and the success of such collaborations.

We may not be successful in generating funds internally or from external sources. If we are unable to obtain additional external funds in 2003, we may be required to delay, scale back or eliminate some or all of our research and development programs.

Contractual Obligations

As of December 31, 2002, our outstanding indebtedness consisted of $1.3 million in principal amount of 9% notes maturing in April 2004. These notes are unsecured. Our only lease commitments relates to our facility in Cambridge, Massachusetts and office equipment acquired under a capital lease which expires in the first half of 2003.

We expect to make capital expenditures of approximately $0.5 million in 2003, principally for the purchase of laboratory and computer equipment.

As of December 31, 2002, our contractual obligations were as follows:

Contractual Obligations	Payments Due by Period			
	Total	Less than 1 year	1-3 years	4-5 years
Debt	$1,306,000	$ —	$1,306,000	$ —
Lease Commitments	2,682,000	645,000	1,222,000	815,000
Employment Agreements	3,689,000	978,000	1,956,000	755,000
Consulting & Collaboration Agreements	243,000	220,000	23,000	—
Total	$7,920,000	$1,843,000	$4,507,000	$1,570,000

FORWARD-LOOKING STATEMENTS

This annual report contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. All statements, other than statements of historical facts, included or incorporated in this report regarding our strategy, future operations, financial position, future revenues, projected costs, prospects, plans and objectives of management are forward-looking statements. The words "believes," "anticipates," "estimates," "plans," "expects," "intends," "may," "projects," "will," and "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We cannot guarantee that we actually will achieve the plans, intentions or expectations disclosed in our forward-looking statements and you should not place undue reliance on our forward-looking statements. In addition, any forward-looking statements represent our estimates only as of the date this annual report is filed with the SEC and should not be relied upon as representing our estimates as of any subsequent date. We do not assume any obligation to update any forward-looking statements. We disclaim any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

RISK FACTORS

There are a number of important factors that could cause our actual results to differ materially from those indicated or implied by forward-looking statements. We believe that the material factors that we discuss below could cause or contribute to such material differences.

Risks Relating to Our Business, Strategy and Industry

If our clinical trials are unsuccessful, or if they are significantly delayed, we may not be able to develop and commercialize our products.

In order to obtain regulatory approvals for the commercial sale of our products, we will be required to complete extensive clinical trials in humans to demonstrate the safety and efficacy of our drug candidates. In 2003, we commenced phase 1 clinical trials in the United Kingdom for HYB2055, our lead IMO compound, and we are currently conducting a phase 1/2 clinical trial of GEM231, our 2nd generation antisense compound for the treatment of cancer. We may not be able to obtain authority from the FDA or other equivalent foreign regulatory agencies to complete these or any clinical trials.

The results from preclinical testing of a drug candidate that is under development may not be predictive of results that will be obtained in human clinical trials. In addition, the results of early human clinical trials may not be predictive of results that will be obtained in larger scale, advanced stage clinical trials. Furthermore, we, one of our collaborators, or a regulatory agency with jurisdiction over the trials, may suspend clinical trials at any time if the subjects or patients participating in such trials are being exposed to unacceptable health risks, or for other reasons. As an example, in 1997, after reviewing the results from the clinical trial of GEM91, our lead antisense compound at the time, we determined not to continue the development of GEM91 and suspended clinical trials of this product candidate.

The rate of completion of clinical trials is dependent in part upon the rate of enrollment of patients. Patient accrual is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the study, the nature of the study, the existence of competitive clinical trials and the availability of alternative treatments. Delays in planned patient enrollment may result in increased costs and prolonged clinical development.

We may not be able to successfully complete any clinical trial of a potential product within any specified time period. In some cases, we may not be able to complete the trial at all. Moreover, clinical trials may not show our potential products to be both safe and efficacious. Thus, the FDA and other regulatory authorities may not approve any of our potential products for any indication.

We face substantial competition which may result in others discovering, developing or commercializing drugs before or more successfully than us.

The biotechnology industry is highly competitive and characterized by rapid and significant technological change. We face, and will continue to face, intense competition from organizations such as pharmaceutical and biotechnology companies, as well as academic and research institutions and government agencies. Some of these organizations are pursuing products based on technologies similar to our technologies. Other of these organizations have developed and are marketing products, or are pursuing other technological approaches designed to produce products, that are competitive with our product candidates in the therapeutic effect these competitive products have on diseases targeted by our product candidates.

Many of our competitors are substantially larger than we are and have greater capital resources, research and development staffs and facilities than we have. In addition, many of our competitors are more experienced than we are in drug discovery, development and commercialization, obtaining regulatory approvals and drug manufacturing and marketing.

We anticipate that the competition with our products and technologies will be based on, among other things, product efficacy, safety, reliability, availability, price and patent position. The timing of market introduction of our products and competitive products will also affect competition among products. We also expect the relative speed with which we can develop products, complete the clinical trials and approval processes and supply commercial quantities of the products to the market to be an important competitive factor. Our competitive position will also depend upon our ability to attract and retain qualified personnel, to obtain patent protection or otherwise develop proprietary products or processes and to secure sufficient capital resources for the period between technological conception and commercial sales.

Because the products that we may develop will be based on new technologies and therapeutic approaches, the market may not be receptive to these products upon their introduction.

The commercial success of any of our products for which we may obtain marketing approval from the FDA or other regulatory authorities will depend upon their acceptance by the medical community and third party payors as clinically useful, cost-effective and safe. Many of the products that we are developing are based upon new technologies or therapeutic approaches that are relatively new and unproven. As a result, it may be more difficult for us to achieve market acceptance of our products. Our efforts to educate the medical community on these potentially unique approaches may require greater resources than would be typically required for products based on conventional technologies or therapeutic approaches. The safety, efficacy, convenience and cost-effectiveness of our products as compared to competitive products will also affect market acceptance.

Competition for technical and management personnel is intense in our industry and we may not be able to sustain our operations or grow if we are unable to attract and retain key personnel.

Our success is highly dependent on the retention of principal members of our technical and management staff, including Stephen Seiler and Sudhir Agrawal. Mr. Seiler, our Chief Executive Officer, has extensive experience in the pharmaceutical industry and as an investment banker and provides strategic leadership for us. The loss of Mr. Seiler's services would be detrimental to the execution of our strategic plan. Dr. Agrawal

serves as our President and Chief Scientific Officer. Dr. Agrawal has made significant contributions to the field of nucleic acid chemistry and is named as an inventor on over 200 U.S. patents and patent applications. Dr. Agrawal provides the scientific leadership for our research and development activities and directly supervises our research staff. The loss of Dr. Agrawal's services would be detrimental to our ongoing scientific progress.

We are a party to employment agreements with each of Mr. Seiler and Dr. Agrawal, but each of these agreements may be terminated by us or the employee for any reason or no reason at any time upon notice to the other party. We do not carry key man life insurance for Mr. Seiler or Dr. Agrawal.

Furthermore, our future growth will require hiring a significant number of qualified technical and management personnel. Accordingly, recruiting and retaining such personnel in the future will be critical to our success. There is intense competition from other companies and research and academic institutions for qualified personnel in the areas of our activities. If we are not able to continue to attract and retain, on acceptable terms, the qualified personnel necessary for the continued development of our business, we may not be able to sustain our operations or grow.

Regulatory Risks

We may not be able to obtain marketing approval for products resulting from our development efforts.

All of the products that we are developing will require additional research and development, extensive preclinical studies and/or clinical trials and regulatory approval prior to any commercial sales. This process is lengthy, often taking a number of years, and is expensive. Since our inception, we have conducted clinical trials of five compounds. In 1997, we determined not to continue clinical development of GEM91. The other four compounds are still in development. Currently, we are conducting clinical trials on two of these compounds, GEM231 and HYB2055.

We may need to address a number of technological challenges in order to complete development of our products. Moreover, these products may not be effective in treating any disease or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining regulatory approval or prevent or limit commercial use.

If we fail to comply with the extensive regulatory requirements to which our products are subject, we could be subject to adverse consequences and penalties.

The testing, manufacturing, labeling, advertising, promotion, export, and marketing, among other things, of our products are subject to extensive regulation by governmental authorities in Europe, the United States, and elsewhere throughout the world.

In general, there can be no assurance that submission of materials requesting permission to conduct clinical trials will result in authorization by the FDA or equivalent foreign regulatory agency to commence clinical trials, or that once clinical trials have begun, testing will be completed successfully within any specific time period, if at all, with respect to any of our products. Once trials are complete and an application for marketing approval has been submitted to the relevant regulatory agency, the regulatory agency may deny the application if applicable regulatory criteria are not satisfied, or may require additional testing or information.

If regulatory approval of a product is granted, such approval may be subject to limitations on the indicated uses for which the product may be marketed or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. As to any product for which we obtain marketing approval, the product, the facilities at which the product is manufactured, any post-approval clinical data and our promotional activities will be subject to continual review and periodic inspections by the FDA and other regulatory agencies.

Both before and after approval is obtained, violations of regulatory requirements may result in various adverse consequences, including the regulatory agency's delay in approving, or refusal to approve a product,

suspension or withdrawal of an approved product from the market, operating restrictions, or the imposition of civil or criminal penalties.

We have only limited experience in regulatory affairs and our products are based on new technologies; these factors may affect our ability or the time we require to obtain necessary regulatory approvals.

We have only limited experience in filing and prosecuting the applications necessary to gain regulatory approvals. Moreover, the products that result from our research and development programs will likely be based on new technologies and new therapeutic approaches that have not been extensively tested in humans. The regulatory requirements governing these types of products may be more rigorous than for conventional drugs. As a result, we may experience a longer regulatory process in connection with any product that we develop based on these new technologies or new therapeutic approaches.

Risks Relating to Our Financial Results and Need for Financing

We have incurred substantial losses and expect to continue to incur losses. We will not be successful unless we reverse this trend.

We have incurred losses in every year since our inception. As of December 31, 2002, we had incurred operating losses of approximately $261.1 million. We expect to continue to incur substantial operating losses in future periods. We have received no revenues from the sale of drugs. To date, almost all of our revenues have been from collaborative and license agreements, interest income and the sale of manufactured synthetic DNA and reagent products by HSP prior to our selling HSP in September 2000. We cannot be certain whether or when we will become profitable because of the significant uncertainties with respect to our ability to generate revenues from the sale of products and from any potential strategic alliances.

We may need additional financing, which may be difficult to obtain. Our failure to obtain necessary financing or doing so on unattractive terms could adversely affect our discovery and development programs and other operations.

We will require substantial funds to conduct research and development, including preclinical testing and clinical trials of our drugs. We will also require substantial funds to conduct regulatory activities and to establish commercial manufacturing, marketing and sales capabilities. Additional financing may not be available when we need it or may not be available on favorable terms.

We believe that, based on our current operating plan, our existing cash resources, after reflecting the stock repurchase, will be sufficient to fund our cash requirements at least through the end of 2003. If we are unable to obtain adequate funding on a timely basis, we may be required to significantly curtail one or more of our discovery or development programs. For example, we significantly curtailed expenditures on our research and development programs during 1999 and 2000 because we did not have sufficient funds available to advance these programs at planned levels. We could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to certain of our technologies, drug candidates or drugs which we would otherwise pursue on our own.

If we raise additional funds by issuing equity securities, further dilution in our then existing stockholders will result. In addition, the terms of the financing may adversely affect the holdings or the rights of such stockholders.

Risks Relating to Collaborators

We need to establish collaborative relationships in order to succeed.

An important element of our business plan is entering into collaborative relationships for the development and commercialization of products based on our discoveries. We face significant competition in seeking appropriate collaborators. Moreover, these arrangements are complex to negotiate and time-consuming to

document. We may not be successful in our efforts to establish collaborative relationships or other alternative arrangements.

Reliance on collaborative relationships poses a number of risks, including the following:

- we cannot effectively control whether our collaborators will devote sufficient resources to our programs or products;
- disputes may arise in the future with respect to the ownership of rights to technology developed with collaborators;
- disagreements with collaborators could delay or terminate the research, development or commercialization of products, or result in litigation or arbitration;
- we may have difficulty enforcing the contracts if one of these collaborators fails to perform;
- our collaborators may terminate their collaborations with us, which could make it difficult for us to attract new collaborators or adversely affect the perception of us in the business or financial communities;
- collaborators have considerable discretion in electing whether to pursue the development of any additional drugs and may pursue technologies or products either on their own or in collaboration with our competitors; and
- collaborators with marketing rights may choose to devote fewer resources to the marketing of our products than they do to products that they develop.

Given these risks, it is possible that any collaborative arrangements into which we enter may not be successful. Previous collaborative arrangements to which we were a party with F. Hoffmann-La Roche and G.D. Searle & Co. both were terminated prior to the development of any product. Failure of these efforts could delay our drug development or impair commercialization of our products.

Risks Relating to Intellectual Property

If we are unable to obtain patent protection for our discoveries, the value of our technology and products will be adversely affected. If we infringe patent or other intellectual property rights of third parties, we may not be able to develop and commercialize our products or the cost of doing so may increase.

Our patent positions, and those of other drug discovery companies, are generally uncertain and involve complex legal, scientific and factual questions.

Our ability to develop and commercialize drugs depends in significant part on our ability to:

- obtain patents;
- obtain licenses to the proprietary rights of others on commercially reasonable terms;
- operate without infringing upon the proprietary rights of others;
- prevent others from infringing on our proprietary rights; and
- protect trade secrets.

We do not know whether any of our patent applications or those patent applications which we license will result in the issuance of any patents. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, invalidated or circumvented, and the rights granted thereunder may not provide us proprietary protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies or duplicate any technology developed by us. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our products can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thus reducing any advantage of

the patent, which could adversely affect our ability to protect future drug development and, consequently, our operating results and financial position.

Third parties may own or control patents or patent applications and require us to seek licenses, which could increase our development and commercialization costs, or prevent us from developing or marketing products.

We may not have rights under some patents or patent applications related to our products. Third parties may own or control these patents and patent applications in the United States and abroad. Therefore, in some cases, to develop, manufacture, sell or import certain of our products, we or our collaborators may choose to seek, or be required to seek, licenses under third party patents issued in the United States and abroad or those that might issue from United States and foreign patent applications. In such event, we would be required to pay license fees or royalties or both to the licensor. If licenses are not available to us on acceptable terms, we or our collaborators may not be able to develop, manufacture, sell or import these products.

We may lose our rights to patents, patent applications or technologies of third parties if our licenses from these third parties are terminated.

We are party to eleven royalty-bearing license agreements under which we have acquired rights to patents, patent applications and technology of third parties. Under these licenses we are obligated to pay royalties on net sales by us of products or processes covered by a valid claim of a patent or patent application licensed to us. We also are required in some cases to pay a specified percentage of any sublicense income that we may receive. These licenses impose various commercialization, sublicensing, insurance and other obligations on us. Our failure to comply with these requirements could result in termination of the licenses. These licenses generally will otherwise remain in effect until the expiration of all valid claims of the patents covered by such licenses or upon earlier termination by the parties. The issued patents covered by these licenses expire at various dates ranging from 2006 to 2021. If one or more of these licenses is terminated, we may be delayed in our efforts to develop and market the products that are covered by the applicable license or licenses.

We may become involved in expensive patent litigation or other proceedings, which could result in our incurring substantial costs and expenses or substantial liability for damages or require us to stop our development and commercialization efforts.

There has been substantial litigation and other proceedings regarding the patent and other intellectual property rights in the biotechnology industry. We may become a party to patent litigation or other proceedings regarding intellectual property rights. For instance, in the fourth quarter of 2002, we became involved in an interference declared by the United States Patent and Trademark Office involving a patent application exclusively licensed by us from UMass and three patents issued to the National Institutes of Health. The cost to us of any patent litigation or other proceeding, including the NIH interference, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the cost of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. If any patent litigation or other proceeding is resolved against us, we or our collaborators may be enjoined from developing, manufacturing, selling or importing our drugs without a license from the other party and we may be held liable for significant damages. We may not be able to obtain any required license on commercially acceptable terms or at all.

Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Patent litigation and other proceedings may also absorb significant management time.

Risks Relating to Product Manufacturing, Marketing and Sales

We have no experience selling, marketing or distributing products and no internal capability to do so.

If we receive regulatory approval to commence commercial sales of any of our products, we will face competition with respect to commercial sales, marketing and distribution. These are areas in which we have no experience. To market any of our products directly, we would need to develop a marketing and sales force with technical expertise and with supporting distribution capability. Alternatively, we could engage a pharmaceutical or other healthcare company with an existing distribution system and direct sales force to assist us. There can be no assurance that we will successfully establish sales and distribution capabilities or gain market acceptance for our products. To the extent we enter co-promotion or other licensing arrangements, any revenues we receive will depend on the efforts of third parties and there can be no assurance that our efforts will succeed. If in the future we elect to perform sales, marketing and distribution functions for such types of products ourselves, we would face a number of additional risks, including the need to recruit a large number of additional experienced marketing and sales personnel.

Because we have limited manufacturing experience, we will be dependent on third-party manufacturers to manufacture products for us or will be required to incur significant costs and devote significant efforts to establish our own manufacturing facilities and capabilities.

We have limited manufacturing experience and no commercial scale manufacturing capabilities. In order to continue to develop our products, apply for regulatory approvals and commercialize products, we will need to develop, contract for or otherwise arrange for the necessary manufacturing capabilities.

We currently rely upon third parties to produce material for preclinical and clinical testing purposes and expect to continue to do so in the future. We also expect to rely upon third parties to produce materials that may be required for the commercial production of our products.

There are a limited number of manufacturers that operate under the FDA's good manufacturing practices regulations capable of manufacturing our products. As a result, we may have difficulty finding manufacturers for our products with adequate capacity for our needs. If we are unable to arrange for third party manufacturing of our products on a timely basis, or to do so on commercially reasonable terms, we may not be able to complete development of our products or market them.

Reliance on third party manufacturers entails risks to which we would not be subject if we manufactured products ourselves, including reliance on the third party for regulatory compliance and quality assurance, the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control, the possibility of termination or nonrenewal of the agreement by the third party, based on its own business priorities, at a time that is costly or inconvenient for us, the potential that third party manufacturers will develop know-how owned by such third party in connection with the production of our products that is necessary for the manufacture of our products and reliance upon third party manufactures to assist us in preventing inadvertent disclosure or theft of our proprietary knowledge.

If we fail to obtain an adequate level of reimbursement for our products by third party payors, there may be no commercially viable markets for our products.

The availability and levels of reimbursement by governmental and other third party payors such as health maintenance organizations, Medicaid, medical insurance companies, medical plan administrators, pharmacy benefit managers, physician and hospital alliances and other physician organizations affect the market for healthcare products. These third party payors continually attempt to contain or reduce the costs of healthcare by challenging the prices charged for medical products and services. We may not be able to sell our products profitably if reimbursement is unavailable or limited in scope or amount.

In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory proposals to change the healthcare system. Further proposals are likely. The potential for adoption

of these proposals affects or will affect our ability to raise capital, obtain collaborators and market our products.

We expect to experience pricing pressures in connection with the sale of our drugs due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative proposals.

We face a risk of product liability claims and may not be able to obtain insurance.

Our business exposes us to the risk of product liability claims that is inherent in the manufacturing, testing and marketing of human therapeutic drugs. Although we have product liability and clinical trial liability insurance that we believe is adequate, this insurance is subject to deductibles and coverage limitations. We may not be able to obtain or maintain adequate protection against potential liabilities. If we are unable to obtain insurance at acceptable cost or otherwise protect against potential product liability claims, we will be exposed to significant liabilities, which may materially and adversely affect our business and financial position. These liabilities could prevent or interfere with our commercialization efforts.

Risks Relating to an Investment in Our Common Stock

Provisions in our charter documents, our rights agreement and provisions of Delaware law may prevent a change in control or management that stockholders may consider desirable.

Section 203 of the Delaware General Corporation Law and our charter, by-laws and rights agreement contain provisions that might enable our management to resist a takeover of our company. These provisions could have the effect of delaying, deferring, or preventing a change in control of us or a change in our management that stockholders may consider favorable or beneficial. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors and take other corporate actions. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock.

Our common stock is considered a "penny stock" and may be difficult to sell.

The SEC has adopted regulations which generally define "penny stock" to be an equity security that has a market price of less than $5.00 per share or an exercise price of less than $5.00 per share, subject to specific exemptions. Presently, the market price of our common stock is substantially less than $5.00 per share and therefore is designated as a "penny stock" according to SEC rules. This designation requires any broker or dealer selling these securities to disclose certain information concerning the transaction, obtain a written agreement from the purchaser and determine that the purchaser is reasonably suitable to purchase the securities. These rules may restrict the ability of brokers or dealers to sell our common stock and may affect the ability of investors to sell their shares. In addition, since our common stock is traded on the OTC Bulletin Board, investors may find it difficult to obtain accurate quotations of our common stock.

Item 7A. ***Quantitative and Qualitative Disclosures About Market Risk***

Historically, our primary exposures have been related to nondollar-denominated operating expenses in Europe. As of December 31, 2002, we have no assets and liabilities related to nondollar-denominated currencies.

We maintain investments in accordance with our investment policy. The primary objectives of our investment activities are to preserve principal, maintain proper liquidity to meet operating needs and maximize yields. Although our investments are subject to credit risk, our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure from any single issue, issuer or type of investments. We do not own derivative financial investment instruments in our investment portfolio.

Based on a hypothetical ten percent adverse movement in interest rates, the potential losses in future earnings, fair value of risk sensitive financial instruments, and cash flows are immaterial, although the actual effects may differ materially from the hypothetical analysis.

Item 8. ***Financial Statements and Supplementary Data***

All financial statements required to be filed hereunder are filed as listed under Item 14(a) immediately after the signature page to this report on Form 10-K, and are incorporated herein by this reference.

Item 9. ***Changes in and Disagreements with Accountants on Accounting and Financial Disclosure***

We previously reported the information required to be reported in this Item in our Current Report on Form 8-K dated April 25, 2002 and filed with the Securities and Exchange Commission on May 1, 2002.

Our consolidated financial statements as of and for the fiscal years ended December 31, 2000 and December 31, 2001 were audited by Arthur Andersen LLP, independent accountants. On August 31, 2002, Arthur Andersen ceased practicing before the SEC. Therefore, Arthur Andersen did not participate in the preparation of this Annual Report on Form 10-K, did not reissue its audit report with respect to the financial statements included in this Annual Report on Form 10-K and did not consent to the inclusion of its audit report in this Annual Report on Form 10-K. As a result, holders of our securities, and investors evaluating offers and purchasing securities pursuant to a prospectus incorporating by reference this Annual Report on Form 10-K, may have no effective remedy against Arthur Andersen in connection with a material misstatement or omission in the financial statements to which its audit report relates. In addition, even if such holders or investors were able to assert such a claim, because it has ceased operations, Arthur Andersen may fail or otherwise have insufficient assets to satisfy claims made by such persons that might arise under federal securities laws or otherwise with respect to Arthur Andersen's audit report.

PART III.

The response to the Part III items incorporate by reference certain sections of Hybridon's Proxy Statement for the Annual Meeting of Stockholders to be held on June 19, 2003, or the 2003 Proxy Statement. The 2003 Proxy Statement will be filed with the Securities and Exchange Commission on or before April 30, 2003.

Item 10. ***Directors and Executive Officers of Hybridon***

The response to this item is contained under the following captions in the 2003 Proxy Statement: "Election of Directors" and "Section 16(a) Beneficial Ownership Reporting Compliance," which sections are incorporated herein by reference. See Part I of this Annual Report on 10-K under the caption "Executive Officers and Key Employees of Hybridon."

Item 11. ***Compensation of Executive Officers***

The response to this item is contained in the 2003 Proxy Statement under the captions: "Certain Transactions," "Director Compensation" and "Executive Compensation" which sections are incorporated herein by reference.

Item 12. ***Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters***

The response to this item is contained in the 2003 Proxy Statement under the caption "Security Ownership of Certain Beneficial Owners and Management," and "Securities Authorized for Issuance Under Equity Compensation Plans", which sections are incorporated herein by reference.

Item 13. ***Certain Relationships and Related Transactions***

The response to this item is contained in the 2003 Proxy Statement under the captions "Certain Transactions," "Director Compensation" and "Executive Compensation," which sections are incorporated herein by reference.

Item 14. ***Controls and Procedures***

Within the 90-day period prior to the filing of this Annual Report on Form 10-K, an evaluation was carried out under the supervision and with the participation of our management, including our Chief Executive Officer, or CEO and Chief Financial Officer, or CFO, of the effectiveness of the design and operation of our disclosure controls and procedures. Based on that evaluation, our CEO and CFO have concluded that our disclosure controls and procedures are designed to ensure that information required to be disclosed by us in reports that we file or submit under the Securities Exchange Act of 1934 is recorded, processed, summarized, and reported within the time periods specified in SEC rules and form and are operating in an effective manner.

There were no significant changes in our internal controls or in other factors that could significantly affect these controls subsequent to the date of their most recent evaluation.

PART IV.

Item 15. ***Exhibits, Financial Statement Schedules and Reports on Form 8-K***

(a) (1) *Financial Statements.*

(2) We are not filing any financial statement schedules as part of this Annual Report on Form 10-K because they are not applicable or the required information is included in the financial statements or notes thereto.

(3) The list of Exhibits filed as a part of this Annual Report on Form 10-K are set forth on the Exhibit Index immediately preceding such Exhibits, and is incorporated herein by this reference.

(b) *Reports on Form 8-K.*

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, on this 27th day of March 2003.

Hybridon, Inc.

By: /s/ STEPHEN R. SEILER
Stephen R. Seiler
Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ JAMES B. WYNGAARDEN, M.D. James B. Wyngaarden, M.D.	Chairman of the Board of Directors	March 27, 2003
/s/ STEPHEN R. SEILER Stephen R. Seiler	Chief Executive Officer and Director (Principal Executive Officer)	March 27, 2003
/s/ SUDHIR AGRAWAL, D. PHIL Sudhir Agrawal, D. Phil	President, Chief Scientific Officer and Director	March 27, 2003
/s/ ROBERT G. ANDERSEN Robert G. Andersen	Chief Financial Officer and Vice President of Operations, Treasurer and Secretary (Principal Financial and Accounting Officer)	March 27, 2003
/s/ YOUSSEF EL-ZEIN Youssef El-Zein	Director	March 27, 2003
/s/ C. KEITH HARTLEY C. Keith Hartley	Director	March 27, 2003
/s/ ANTHONY GEORGES MARCEL, M.D., PHD. Anthony Georges Marcel, M.D., PhD.	Director	March 27, 2003
/s/ WILLIAM REARDON, C.P.A. William Reardon, C.P.A.	Director	March 27, 2003
/s/ PAUL C. ZAMECNIK, M.D. Paul C. Zamecnik, M.D.	Director	March 27, 2003

I, Stephen R. Seiler, certify that:

1. I have reviewed this annual report on Form 10-K of Hybridon, Inc.;

2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;

3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this annual report;

4. The registrant's other certifying officers and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-14 and 15d-14) for the registrant and we have:

   a) designed such disclosure controls and procedures to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this annual report is being prepared;

   b) evaluated the effectiveness of the registrant's disclosure controls and procedures as of a date within 90 days prior to the filing date of this annual report (the "Evaluation Date"); and

   c) presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures based on our evaluation as of the Evaluation Date;

5. The registrant's other certifying officers and I have disclosed, based on our most recent evaluation, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent function):

   a) all significant deficiencies in the design or operation of internal controls which could adversely affect the registrant's ability to record, process, summarize and report financial data and have identified for the registrant's auditors any material weaknesses in internal controls; and

   b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls; and

6. The registrant's other certifying officers and I have indicated in this annual report whether or not there were significant changes in internal controls or in other factors that could significantly affect internal controls subsequent to the date of our most recent evaluation, including any corrective actions with regard to significant deficiencies and material weaknesses.

/s/ Stephen R. Seiler

Stephen R. Seiler
Chief Executive Officer

Dated: March 27, 2003

I, Robert G. Andersen certify that:

1. I have reviewed this annual report on Form 10-K of Hybridon, Inc.;

2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;

3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this annual report;

4. The registrant's other certifying officers and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-14 and 15d-14) for the registrant and we have:

   a) designed such disclosure controls and procedures to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this annual report is being prepared;

   b) evaluated the effectiveness of the registrant's disclosure controls and procedures as of a date within 90 days prior to the filing date of this annual report (the "Evaluation Date"); and

   c) presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures based on our evaluation as of the Evaluation Date;

5. The registrant's other certifying officers and I have disclosed, based on our most recent evaluation, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent function):

   a) all significant deficiencies in the design or operation of internal controls which could adversely affect the registrant's ability to record, process, summarize and report financial data and have identified for the registrant's auditors any material weaknesses in internal controls; and

   b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls; and

6. The registrant's other certifying officers and I have indicated in this annual report whether or not there were significant changes in internal controls or in other factors that could significantly affect internal controls subsequent to the date of our most recent evaluation, including any corrective actions with regard to significant deficiencies and material weaknesses.

/s/ Robert G. Andersen

Robert G. Andersen
Chief Financial Officer

Dated: March 27, 2003

HYBRIDON, INC. AND SUBSIDIARIES

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS
December 31, 2002

REPORT OF INDEPENDENT AUDITORS

The Board of Directors and Stockholders
Hybridon, Inc.

We have audited the accompanying balance sheet of Hybridon, Inc. as of December 31, 2002, and the related statement of operations, stockholders' equity, and cash flows for the year then ended. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audit. The financial statements of Hybridon, Inc. as of December 31, 2001 and for each of the two years in the period then ended were audited by other auditors who have ceased operations and whose report dated February 21, 2002, expressed an unqualified opinion on those statements.

We conducted our audit in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Hybridon, Inc. at December 31, 2002 and the results of its operations and its cash flows for the year then ended in conformity with accounting principles generally accepted in the United States.

As discussed above, the financial statements of Hybridon, Inc. as of December 31, 2001 and for each of the two years in the period then ended were audited by other auditors who have ceased operations. As described in Note 2(d), in 2002 the Company reclassified the proceeds from the 2001 sale of certain securities designated as trading securities from cash flows from investing activities to cash flows from operating activities; disclosed the separate components of net property and equipment as of December 31, 2001; and disclosed separately the weighted average grant date fair value and exercise price of stock options granted with exercise prices equal to, exceeding or less than market price on the grant date in 2001 and 2000. The 2001 and 2000 financial statements have been revised to reflect the reclassification and additional disclosures described above. We audited the adjustment that was applied in 2001 to reflect the reclassification and the additional disclosures in 2001 and 2000 as described below.

With respect to the trading securities adjustment, we (a) agreed the 2001 receipt of 857,143 shares of Isis Pharmaceuticals, Inc. ("Isis") common stock to the Company's 2001 independent broker statement; and (b) agreed the 2001 proceeds of $15,619,475 from the sale of the aforementioned shares of Isis common stock to the Company's 2001 independent broker statement and agreed such amount to the amount presented as proceeds from sale of trading securities in the 2001 Consolidated Statement of Cash Flows. With respect to the separate components of net property and equipment, we (a) tested the mathematical accuracy of the separately reported components of net property and equipment as of December 31, 2001 reported in Note 4; and (b) agreed such components to the Company's underlying records obtained from management and certified by management to a third party. With respect to the stock option grants, we (a) agreed the separately reported weighted average grant date fair value and exercise price of stock options granted in 2001 and 2000 reported in Note 2(k) to a schedule prepared by the Company from its underlying records; (b) agreed the information contained in the aforementioned schedule to the signed minutes of the 2000 and 2001 Board of Directors and Compensation Committee meetings; and (c) reconciled the number of stock options listed as granted within the aforementioned schedule to the number of stock options listed as granted in Note 10(d).

In our opinion, such adjustment and additional disclosures are appropriate and have been properly applied. However, we were not engaged to audit, review, or apply any procedures to the 2001 and 2000 financial statements of the Company other than with respect to such adjustment and additional disclosures as described in Note 2(d) and, accordingly, we do not express an opinion or any other form of assurance on the 2001 and 2000 financial statements taken as a whole.

/s/ Ernst & Young LLP

Boston, Massachusetts
January 23, 2003, except for Note 18,
as to which the date is February 14, 2003

THE FOLLOWING REPORT IS A COPY OF A REPORT PREVIOUSLY ISSUED BY ARTHUR ANDERSEN LLP AND HAS NOT BEEN REISSUED BY ARTHUR ANDERSEN LLP.

REPORT OF INDEPENDENT PUBLIC ACCOUNTANTS

To Hybridon, Inc.:

We have audited the accompanying consolidated balance sheets of Hybridon, Inc. (a Delaware corporation) as of December 31, 2001 and 2000, and the related consolidated statements of operations, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2001. These financial statements are the responsibility of Hybridon, Inc.'s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Hybridon, Inc. and subsidiaries as of December 31, 2001 and 2000, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2001, in conformity with accounting principles generally accepted in the United States.

/s/ ARTHUR ANDERSEN LLP

Boston, Massachusetts
February 21, 2002

HYBRIDON, INC. AND SUBSIDIARIES

CONSOLIDATED BALANCE SHEETS

	December 31, 2002	December 31, 2001
ASSETS		
Current assets:		
Cash and cash equivalents	$ 4,527,500	$ 20,923,295
Short-term investments	14,647,417	10,910,987
Receivables	406,313	274,863
Prepaid expenses and other current assets	191,770	56,992
Total current assets	19,773,000	32,166,137
Long-term investments	941,069	—
Property and equipment, net	534,764	143,298
Total Assets	$ 21,248,833	$ 32,309,435
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 831,192	$ 498,642
Accrued expenses	828,227	1,021,660
Current portion of long-term debt	—	288,028
Current portion of capital lease	33,591	—
Current portion of deferred revenue	442,333	3,098,654
Total current liabilities	2,135,343	4,906,984
9% convertible subordinated notes payable	1,306,000	1,306,000
Deferred revenue, net of current portion	363,360	26,129,725
Commitments and contingencies		
Stockholders' equity (deficit):		
Preferred stock, $0.01 par value		
Authorized — 5,000,000 shares		
Series A convertible preferred stock		
Designated — 1,500,000 shares		
Issued and outstanding — 678,362 and 640,166 shares at December 31, 2002 and 2001, respectively		
Liquidation value — $68,909,744 at December 31, 2002	6,784	6,402
Common stock, $0.001 par value		
Authorized — 150,000,000 shares		
Issued and outstanding — 47,944,857 and 45,632,525 shares at December 31, 2002 and 2001, respectively	47,945	45,632
Additional paid-in capital	278,578,678	273,870,458
Accumulated deficit	(261,142,926)	(273,868,184)
Accumulated other comprehensive loss	(1,944)	—
Deferred compensation	(44,407)	(87,582)
Total stockholders' equity (deficit)	17,444,130	(33,274)
Total Liabilities and Stockholders' Equity (Deficit)	$ 21,248,833	$ 32,309,435

The accompanying notes are an integral part of these consolidated financial statements.

HYBRIDON, INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF OPERATIONS

	Years Ended December 31,		
	2002	2001	2000
Revenues:			
License fees	$29,549,836	$ 987,556	$ 179,277
Research and development	10,375	—	—
Royalty and other income	45,719	134,225	82,826
Service revenue	—	—	82,500
Investment income	649,554	577,267	228,695
Total revenues	30,255,484	1,699,048	573,298
Operating expenses:			
Research and development	7,877,343	4,868,035	3,620,203
General and administrative	7,054,023	5,051,344	3,184,017
Stock-based compensation from repriced options (1)	(1,297,445)	1,761,657	—
Interest	150,023	1,319,387	2,153,831
Total operating expenses	13,783,944	13,000,423	8,958,051
Gain on sale of securities, net	—	5,217,451	—
Income (loss) from continuing operations	16,471,540	(6,083,924)	(8,384,753)
Income from discontinued operations	—	2,662,597	5,462,154
Income (loss) before provision for income taxes and extraordinary item	16,471,540	(3,421,327)	(2,922,599)
Income tax credit (provision)	500,000	(500,000)	—
Income (loss) before extraordinary item	16,971,540	(3,921,327)	(2,922,599)
Extraordinary item:			
Loss on conversion of 8% convertible subordinated notes payable	—	(1,411,876)	—
Net income (loss)	16,971,540	(5,333,203)	(2,922,599)
Accretion of preferred stock dividends	(4,246,282)	(8,341,935)	(4,087,317)
Net income (loss) applicable to common stockholders	$12,725,258	$(13,675,138)	$(7,009,916)
Income (loss) per share from continuing operations:			
Basic	$ 0.36	$ (0.21)	$ (0.48)
Diluted	$ 0.32	$ (0.21)	$ (0.48)
Net income (loss) per share:			
Basic	$ 0.27	$ (0.44)	$ (0.40)
Diluted	$ 0.24	$ (0.44)	$ (0.40)
Shares used in computing basic net income (loss) per common share	46,879,232	30,820,098	17,418,233
Shares used in computing diluted net income (loss) per common share	52,984,415	30,820,098	17,418,233
(1) The following summarizes the allocation of stock based compensation from repriced options			
Research and development	$ (925,210)	$ 1,060,404	$ —
General and administrative	(372,235)	701,253	—
Total	$(1,297,445)	$ 1,761,657	$ —

The accompanying notes are an integral part of these consolidated financial statements.

HYBRIDON, INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock						
	Number Of Shares	$0.01 Par Value	Number Of Shares	$0.01 Par Value	Number Of Shares	$0.001 Par Value	Additional Paid-In Capital	Other Comprehensive Income (Loss)	Accumulated Deficit	Deferred Compensation	Total Stockholders' Equity (Deficit)
Balance, December 31, 1999	661,856	$6,618	—	$ —	16,260,722	$16,261	$247,813,331	$ —	$(253,183,130)	$(725,383)	$(6,072,303)
Exercise of common stock options	—	—	—	—	335,240	336	167,287	—	—	—	167,623
Retirement of common stock	—	—	—	—	(250,000)	(250)	—	—	—	—	(250)
Cancellation of stock options	—	—	—	—	—	—	(50,781)	—	—	50,781	—
Revaluation of stock options issued to non-employees	—	—	—	—	—	—	(449,665)	—	—	449,665	—
Preferred stock dividends	41,363	414	—	—	—	—	4,086,903	—	(4,087,317)	—	—
Issuance of stock options to non-employees	—	—	—	—	—	—	117,523	—	—	—	117,523
Issuance of warrants in connection with line of credit	—	—	—	—	—	—	731,136	—	—	—	731,136
Conversion of debt into common stock	—	—	—	—	214,043	214	230,953	—	—	—	231,167
Conversion of preferred into common stock	(77,049)	(770)	—	—	1,822,232	1,821	(1,051)	—	—	—	—
Amortization of deferred compensation	—	—	—	—	—	—	—	—	—	217,701	217,701
Net loss	—	—	—	—	—	—	—	—	(2,922,599)	—	(2,922,599)
Balance, December 31, 2000	626,170	6,262	—	—	18,382,237	18,382	252,645,636	—	(260,193,046)	(7,236)	(7,530,002)
Exercise of common stock options and warrants	—	—	—	—	4,965,715	4,966	312,228	—	—	—	317,194
Sale of common stock	—	—	—	—	510,000	510	427,890	—	—	—	428,400
Issuance of stock, stock options and warrants for services	—	—	—	—	298,530	298	898,269	—	—	(10,756)	887,811
Issuance of stock bonus	—	—	—	—	157,471	157	88,419	—	—	—	88,576
Issuance of stock options to employees	—	—	—	—	—	—	112,192	—	—	(112,192)	—
Amortization of deferred compensation	—	—	—	—	—	—	—	—	—	42,602	42,602
Conversion of 8% notes into stock	—	—	76,046	760	1,140,448	1,140	9,301,791	—	—	—	9,303,691
Preferred stock dividends	40,075	401	2,213	22	—	—	8,341,512	—	(8,341,935)	—	—
Conversion of preferred into common stock	(26,079)	(261)	(78,259)	(782)	20,178,124	20,179	(19,136)	—	—	—	—
Stock-based compensation from repriced options	—	—	—	—	—	—	1,761,657	—	—	—	1,761,657
Net loss	—	—	—	—	—	—	—	—	(5,333,203)	—	(5,333,203)
Balance, December 31, 2001	640,166	6,402	—	—	45,632,525	45,632	273,870,458	—	(273,868,184)	(87,582)	(33,274)
Exercise of common stock options and warrants	—	—	—	—	1,162,172	1,162	458,514	—	—	—	459,676
Issuance of stock under the Isis Agreement and warrants	—	—	—	—	1,005,499	1,006	1,263,664	—	—	—	1,264,670
Issuance of stock options to employees	—	—	—	—	—	—	6,150	—	—	(6,150)	—
Amortization of deferred compensation	—	—	—	—	—	—	—	—	—	49,325	49,325
Conversion of 8% notes into stock	—	—	—	—	52,637	53	31,529	—	—	—	31,582
Preferred stock dividends	42,107	421	—	—	—	—	4,245,861	—	(4,246,282)	—	—
Conversion of preferred into common stock	(3,911)	(39)	—	—	92,024	92	(53)	—	—	—	—
Stock-based compensation from repriced options	—	—	—	—	—	—	(1,297,445)	—	—	—	(1,297,445)
Comprehensive income:											
Unrealized loss on marketable securities	—	—	—	—	—	—	—	(1,944)	—	—	(1,944)
Net income	—	—	—	—	—	—	—	—	16,971,540	—	16,971,540
Total comprehensive income	—	—	—	—	—	—	—	—	—	—	16,969,596
Balance, December 31, 2002	678,362	$6,784	—	$ —	47,944,857	$47,945	$278,578,678	$(1,944)	$(261,142,926)	$ (44,407)	$17,444,130

The accompanying notes are an integral part of these consolidated financial statements.

HYBRIDON, INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Years Ended December 31,		
	2002	2001	2000
Cash Flows From Operating Activities:			
Net income (loss)	$ 16,971,540	$ (5,333,203)	$(2,922,599)
Income from discontinued operations	—	2,662,597	5,462,154
Income (loss) from continuing operations, including extraordinary item	16,971,540	(7,995,800)	(8,384,753)
Adjustments to reconcile net loss to net cash used in operating activities —			
Extraordinary loss on exchange of 8% convertible subordinated notes payable	—	1,411,876	—
Proceeds from trading securities, net	—	15,619,475	—
Gain on sale of property and equipment	—	(45,560)	—
Realized loss on trading securities	—	1,664,810	—
Stock-based compensation	(1,297,445)	1,850,233	117,523
Depreciation and amortization expense	552,115	37,703	115,403
Amortization of deferred compensation	49,325	42,602	217,701
Amortization of deferred financing costs	10,586	162,465	456,919
Issuance of common stock warrants	98,290	—	731,136
Issuance of common stock	1,166,379	—	—
Non cash interest expense	21,882	912,224	151,077
Issuance of common stock for services rendered	—	177,786	—
Changes in operating assets and liabilities —			
Receivables	(131,450)	(243,351)	(140,875)
Prepaid expenses and other current assets	(145,364)	(6,301)	30,298
Accounts payable and accrued expenses	144,892	(506,387)	(935,000)
Deferred revenue	(28,422,685)	12,654,116	—
Net cash (used in) provided by continuing operating activities	(10,981,935)	25,735,891	(7,640,571)
Net cash provided by discontinued operations	—	3,000,000	11,563,672
Cash Flows From Investing Activities:			
Purchases of held-to-maturity securities	(14,582,249)	(13,653,578)	(2,000,000)
Purchases of available-for-sale securities	(1,419,615)	—	—
Proceeds from sale of held-to-maturity securities	3,047,725	—	—
Proceeds from maturities of held-to-maturity securities	7,816,000	—	—
Proceeds from sale and maturities of securities, net	—	4,607,995	—
Purchases of property and equipment	(371,584)	(90,322)	(35,572)
Proceeds from sale of property and equipment	—	45,560	—
Increase in other assets	—	—	(101,401)
Net cash used in investing activities	(5,509,723)	(9,090,345)	(2,136,973)
Cash Flows From Financing Activities:			
Proceeds from exercise of common stock options and warrants	459,676	317,194	—
Payments on debt	(284,102)	(6,000,000)	—
Payments on capital lease	(79,711)	—	—
Net proceeds from sale of common stock	—	428,400	167,623
Decrease (increase) in restricted cash	—	5,000,000	(5,000,000)
Proceeds from issuance of convertible notes payable and warrants	—	—	1,795,566
Net borrowings under line of credit	—	—	231,167
Net cash provided by (used in) financing activities	95,863	(254,406)	(2,805,644)
Net (decrease) increase in cash and cash equivalents	(16,395,795)	19,391,140	(1,019,516)
Cash and cash equivalents, beginning of period	20,923,295	1,532,155	2,551,671
Cash and cash equivalents, end of period	$ 4,527,500	$ 20,923,295	$ 1,532,155

The accompanying notes are an integral part of these consolidated financial statements.

(1) Organization

Hybridon, Inc. (the Company) was incorporated in the State of Delaware on May 25, 1989. The Company is engaged in the discovery and development of novel therapeutics and diagnostics using synthetic DNA. The Company's activities are based on four technologies: CpG-like immunomodulatory oligonucleotide (IMO) technology, which uses synthetic DNA that contain specific sequences that mimic bacterial DNA to modulate responses of the immune system; antisense technology, which uses synthetic DNA to block the production of disease causing proteins at the cellular level; cancer therapy potentiation technology, which uses synthetic DNA to enhance the antitumor activity of certain marketed anticancer drugs and increase their effectiveness; and Cyclicon technology, which uses novel synthetic DNA structures for identifying gene function in drug target validation and drug discovery.

Since inception, the Company has been primarily engaged in research and development and manufacturing. To date, all revenues received by the Company have been from collaboration and licensing agreements, interest income on investment funds, and manufacturing of synthetic DNA and reagent products by the Company's Hybridon Specialty Products or HSP, business prior to its disposal in September 2000 (see Note 14).

(2) Summary of Significant Accounting Policies

(a) Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

The Company is subject to a number of risks and uncertainties similar to those of other companies of the same size within the biotechnology industry, such as uncertainty of clinical trial outcomes, uncertainty of additional funding and history of operating losses.

(b) Cash Equivalents and Short-Term Investments

The Company considers all highly liquid investments with maturities of 90 days or less when purchased to be cash equivalents. Cash and cash equivalents at December 31, 2002 and 2001 consist of the following:

	December 31,	
	2002	2001
Cash and cash equivalents		
Cash and money market funds	$2,527,500	$20,923,295
Corporate bonds	2,000,000	—
Total	$4,527,500	$20,923,295

The Company accounts for investments in accordance with Statement of Financial Accounting Standards (SFAS) No. 115, *Accounting for Certain Investments in Debt and Equity Securities.* Management determines the appropriate classification of marketable securities at the time of purchase. In accordance with SFAS No. 115, investments that the Company has the positive intent and ability to hold to maturity are classified as "held to maturity" and reported at amortized cost, adjusted for amortization of premiums and accretion of discounts to maturity, which approximates fair market value. Such amortization is included in "Investment income" on the accompanying consolidated statement of operations. Investments that the Company does not

have the positive intent to hold to maturity are classified as "available-for-sale" and reported at fair market value. Unrealized gains and losses associated with "available-for-sale" investments are recorded in "Accumulated other comprehensive loss" on the accompanying consolidated balance sheet. The amortization of premiums and accretion of discounts, and any realized gains and losses and declines in value judged to be other than temporary, and interest and dividends are included in "Investment income" on the accompanying consolidated statement of operations for all available-for-sale securities. The cost of securities sold is based on the specific identification method. For the year ended December 31, 2002, there were no realized gains or losses or permanent declines in value that were included in "Investment income" on the accompanying consolidated statement of operations.

During 2002, the Company sold three of its securities issued by two corporations which the Company had classified as "held-to-maturity" as of December 31, 2001. The Company sold such securities when the underlying corporations' credit ratings were down-graded. In order to avoid incurring any potential losses, the Company sold these securities for approximately $3,048,000 which was their approximate book value.

Short-term investments have maturities of greater than three months and mature within one year of the balance sheet date. All of the short-term investments mature prior to December 31, 2003. The long-term investment held at December 31, 2002 matures in the first quarter of 2004. There were no long-term investments at December 31, 2001. At December 31, 2002 and December 31, 2001, the Company's investments consisted of the following:

	December 31,	
	2002	2001
Short-term investments		
Held-to-maturity at amortized cost:		
Government bonds	$10,047,377	$ 8,928,847
Corporate bonds	4,136,666	1,982,140
Available-for-sale corporate bonds at market	463,374	—
Total short-term investments	14,647,417	10,910,987
Long-term available-for-sale corporate bonds	941,069	—
Total	$15,588,486	$10,910,987

The following is a summary of available-for-sale securities:

	December 31, 2002			
	Cost	Gross Unrealized Losses	Gross Unrealized Gains	Estimated Fair Value
Corporate bonds:				
Due in one year or less	$ 462,346	$ —	$1,028	$ 463,374
Due in one to two years	944,041	2,972	—	941,069
Total available-for-sale securities	$1,406,387	$2,972	$1,028	$1,404,443

Shares received in 2001 in connection with the license agreement discussed in Note 7(a) were classified as trading securities in accordance with SFAS No. 115, as the Company's intent was to sell the securities in the short-term. Trading securities are reported at fair value with the changes to the fair value being reported in earnings. Upon execution of the hedging contracts discussed in Note 7(a), the gains or losses on these securities were offset completely by the losses or gains on the hedging contracts. The Company recorded

approximately $306,000 in hedging contract expenses which were included in the gain on sale of securities. In 2001, the Company also recognized $1,359,000 in losses on trading securities. All trading securities were sold prior to December 31, 2001.

(c) Depreciation and Amortization

Depreciation and amortization are computed using the straight-line method based on the estimated useful lives of the related assets, as follows:

Asset Classification	Estimated Useful Life
Leasehold improvements	Life of lease
Laboratory equipment and other	3 – 5 years

(d) Reclassification and Additional Disclosures

Certain amounts in the prior years consolidated financial statements have been reclassified and certain additional disclosures have been made to such financial statements as discussed below.

The Company reclassified the proceeds from the 2001 sale of certain securities designated as trading securities (see Note 2(b)) from cash flows from investing activities to cash flows from operating activities in the Consolidated Statement of Cash Flows for the year ended December 31, 2001.

The Company disclosed the separate components of net property and equipment as of December 31, 2001 (see Note 4) and disclosed separately the weighted average grant date fair value and exercise price of stock options granted with exercise prices equal to, exceeding or less than market price on the grant date in 2001 and 2000 (see Note 2(k)).

(e) Revenue Recognition

In December 1999, the Securities and Exchange Commission issued Staff Accounting Bulletin (SAB) No. 101, *Revenue Recognition*. This bulletin summarizes views of the Staff on applying accounting principles generally accepted in the United States to revenue recognition in financial statements. The Company's revenue recognition policy complies with SAB No. 101.

License fees and other upfront fees, not specifically tied to a separate earnings process, are recognized ratably over the term of the contract or the term in which the Company must fulfill an obligation to aid in the research or use of the licensed technology.

Service and research and development revenue is recognized when the services are performed.

For payments that are specifically associated with a separate earnings process, revenue will be recognized when the specific performance obligation is completed. Performance obligations typically consist of significant milestones in the development life cycle of the related technology, such as initiation of clinical trials, filing for approval with regulatory agencies and approvals by regulatory agencies.

Royalty income represents amounts earned under certain collaboration and license agreements and is recognized as earned, which generally occurs upon receipt of quarterly royalty statements from the licensee or, in the case of a contractually-stated minimum annual royalty arrangement, the greater of the amount actually earned or the guaranteed minimum amount.

Interest income, which also includes the amortization of debt discounts and premiums, is recognized as earned based upon the terms of the underlying security.

(f) Financial Instruments

SFAS No. 107, *Disclosures About Fair Value of Financial Instruments*, requires disclosure of the estimated fair values of financial instruments. The Company's financial instruments consist of cash and cash equivalents, short-term investments, receivables and debt obligations. The estimated fair values of these financial instruments approximates their carrying values as of December 31, 2002 and 2001, respectively. The estimated fair values have been determined through information obtained from market sources and management estimates. As of December 31, 2002 and 2001, the Company does not have any material derivative or any other financial instruments as defined by SFAS No. 133, *Accounting for Derivative and Hedging Instruments.*

(g) Comprehensive Loss

The Company applies SFAS No. 130, *Reporting Comprehensive Income*. Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from nonowner sources. Comprehensive income for the year ended December 31, 2002 is comprised of reported net income and net unrealized losses on investments included in "Accumulated other comprehensive loss" on the accompanying consolidated balance sheet. The Company's comprehensive loss is the same as the reported net loss for the years ended December 31, 2001 and 2000.

(h) Net Income (Loss) per Common Share

The Company applies SFAS No. 128, *Earnings per Share*. Under SFAS No. 128, basic and diluted net income (loss) per common share is computed using the weighted average number of shares of common stock outstanding during the period. In addition, diluted net income per common share is calculated to give effect of stock options, convertible preferred stock and convertible debt (where the effect is not antidilutive) resulting in lower net income per share. The dilutive effect of outstanding stock options is reflected by the application of the treasury stock method under SFAS No. 128. Diluted net loss per common share is the same as basic net loss per common share for the years ended December 31, 2001 and 2000 as the effects of the Company's potential common stock equivalents are antidilutive (see Note 15).

(i) Segment Reporting

SFAS No. 131, *Disclosures About Segments of an Enterprise and Related Information*, establishes standards for reporting information regarding operating segments in annual financial statements and requires selected information for those segments to be presented in interim financial reports issued to stockholders. SFAS No. 131 also establishes standards for related disclosures about products and services and geographic areas. To date, the Company has viewed its operations and manages its business as one operating segment. Accordingly, the Company operates in one segment, which is the business of discovering and developing novel therapeutics through the application of synthetic DNA. As a result, the financial information disclosed herein represents all of the material financial information related to the Company's principal operating segment. For all of the periods presented, all of the Company's revenues were generated in the United States. As of December 31, 2002 and 2001, all assets were located in the United States.

(j) Derivative Instruments and Hedging

The Company applies SFAS No. 133, *Accounting for Derivative Instruments and Hedging Activities*, as amended by SFAS Nos. 137 and 138. These statements establish accounting and reporting standards for derivative instruments, including derivative instruments embedded in other contracts and for hedging activities. In addition, the Emerging Issues Task Force (EITF) has issued a number of derivative-related tentative and final consensuses. The Company did not own any derivative instruments at December 31, 2002

and 2001. During 2001, the Company did enter into hedging contracts, all of which expired prior to December 31, 2001 (see Note 7(a)).

(k) Stock-Based Compensation

The Company applies the disclosure only provisions of SFAS No. 123, *Accounting for Stock-Based Compensation*. The Company continues to account for employee stock compensation at intrinsic value, in accordance with Accounting Principles Board (APB) Opinion No. 25, *Accounting for Stock Issued to Employees* and related interpretations, with disclosure of the effects of fair value accounting on net income or net loss and related per share amounts on a pro forma basis.

The Company has computed the pro forma disclosures required by SFAS No. 123 for all stock options and warrants granted to employees after January 1, 1995, using the Black-Scholes option-pricing model. The assumptions used for the years ended December 31, 2002, 2001, and 2000 are as follows:

	2002	2001	2000
Average risk free interest rate	4.23%	4.77%	6.39%
Expected dividend yield	—	—	—
Expected lives	6 years	6 years	6 years
Expected volatility	90%	90%	90%
Weighted average grant date fair value of options granted during the period (per share)	$ 0.70	$ 0.59	$ 0.98

For the years ended December 31, 2002, 2001 and 2000, the weighted average per share grant date fair value and exercise price per share of option grants to employees in relation to market price of the stock on the date of the grant is as follows:

	Exercise Price		
	Equals Market Price	Exceeds Market Price	Is Less than Market Price
2002 Option Grants			
Weighted average grant date fair value of options granted during the period	$0.62	$1.12	$1.11
Weighted average exercise price of options granted during the period	$0.82	$1.54	$1.40
2001 Option Grants			
Weighted average grant date fair value of options granted during the period	$0.57	$0.36	$0.65
Weighted average exercise price of options granted during the period	$0.75	$1.06	$0.81
2000 Option Grants			
Weighted average grant date fair value of options granted during the period	$1.01	$0.79	—
Weighted average exercise price of options granted during the period	$1.29	$1.07	—

The Black-Scholes option-pricing model was developed for use in estimating the fair value of traded options, which have no vesting restrictions and are fully transferable. In addition, option-pricing models require the input of highly subjective assumptions including expected stock price volatility. Because the

Company's employee stock options have characteristics significantly different from those of traded options, and because changes in the subjective input assumptions can materially affect the fair value estimate, in management's opinion, the existing models do not necessarily provide a reliable single measure of the fair value of its employee stock options.

The pro forma effect of applying SFAS No. 123 for the three years ended December 31, 2002 would be as follows:

	2002	2001	2000
Net income (loss) applicable to common stockholders, as reported	$12,725,258	$(13,675,138)	$(7,009,916)
Less: stock-based compensation (income) expense included in reported net income (loss)	(1,297,445)	1,761,657	—
Add: stock-based employee compensation expense determined under fair value based method for all awards	(1,586,526)	(2,215,259)	(1,379,089)
Pro forma net income (loss) applicable to common stockholders, as adjusted for the effect of applying SFAS No. 123.	$ 9,841,287	$(14,128,740)	$(8,389,005)
Basic net income (loss) per common shares —			
As reported	$ 0.27	$ (0.44)	$ (0.40)
Pro forma	$ 0.21	$ (0.46)	$ (0.48)
Diluted net income (loss) per common shares —			
As reported	$ 0.24	$ (0.44)	$ (0.40)
Pro forma	$ 0.19	$ (0.46)	$ (0.48)

The effects on years ended December 31, 2002, 2001 and 2000 pro forma net income (loss) and net income (loss) per share of expensing the estimated fair value of stock options are not necessarily representative of the effects on reported net income (loss) for future years because of the vesting period of the stock options and the potential for issuance of additional stock options in future years.

(l) New Accounting Pronouncements

In August 2001, the FASB issued SFAS No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets*. This statement supercedes SFAS No. 121, *Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to Be Disposed Of,* and the accounting and reporting provisions of APB Opinion No. 30, *Reporting the Results of Operations — Reporting the Effects of Disposal of a Segment of a Business, and Extraordinary, Unusual and Infrequently Occurring Events and Transactions*. Under this statement, it is required that one accounting model be used for long-lived assets to be disposed of by sale, whether previously held and used or newly acquired, and it broadens the presentation of discontinued operations to include more disposal transactions. The provisions of this statement are effective for financial statements issued for fiscal years beginning after December 15, 2001, and interim periods within those fiscal years, with early adoption permitted. The adoption of SFAS 144 did not have a material impact on the Company's consolidated financial statements.

In April 2002, the Financial Accounting Standards Board issued Statement of Financial Accounting Standards No. 145, (FAS 145), *Rescission of FASB Statements No. 4, 44 and 64, Amendment of FASB*

Statement No. 13, and Technical Corrections. Under FAS 145, gains and losses on extinguishments of debt are to be classified as income or loss from continuing operations rather than extraordinary items. The Company is required to adopt FAS 145 in the first quarter of fiscal 2003; accordingly, operating results for the first quarter of 2001 will be restated to include the $1.4 million loss discussed in Note 6(c) that was previously classified as an extraordinary item.

In November 2002, the FASB issued Interpretation No. 45 (or FIN 45), *Guarantor's Accounting and Disclosure Requirements for Guarantees, Including Indirect Guarantees of Indebtedness of Others*. FIN 45 elaborates on the existing disclosure requirements for most guarantees, including residual value guarantees issued in conjunction with operating lease agreements. It also clarifies that at the time a company issues a guarantee, the company must recognize an initial liability for the fair value of the obligation it assumes under that guarantee and must disclose that information in its interim and annual financial statements. The initial recognition and measurement provisions apply on a prospective basis to guarantees issued or modified after December 31, 2002. The disclosure requirements are effective for financial statements of interim or annual periods ending after December 15, 2002. The Company is currently assessing the impact of the initial recognition and measurement provisions on its financial statements.

In December 2002, the FASB issued Statement No. 148, *Accounting for Stock-Based Compensation — Transition and Disclosure*. FAS 148 amends FAS 123 *Accounting for Stock-Based Compensation* to provide alternative methods of transition for a voluntary change to the fair value based method of accounting for stock-based employee compensation. In addition, FAS 148 amends the disclosure requirements of FAS 123 to require more prominent disclosures in both annual and interim financial statements about the method of accounting for stock-based employee compensation and the effect of the method used on reported results. The additional disclosure requirements of FAS 148 are effective for fiscal years ending after December 15, 2002 and are included in Note 2(k).

The Emerging Issues Task Force reached a consensus on EITF 00-21, *Accounting for Revenue Arrangements with Multiple Deliverables* at the November 21, 2002 meeting, which addresses how to account for arrangements that may involve the delivery or performance of multiple products, services, and/or rights to use assets. The final consensus will be applicable to agreements entered into in fiscal periods beginning after June 15, 2003 with early adoption permitted. Additionally, companies will be permitted to apply the consensus guidance to all existing arrangements as the cumulative effect of a change in accounting principle in accordance with APB Opinion No. 20, Accounting Changes.

Under EITF 00-21 revenue arrangements with multiple deliverables should be divided into separate units of accounting if the deliverables in the arrangement meet the following criteria: (1) the delivered item(s) has value to the customer on a standalone basis; item(s) has value on a standalone basis if it is sold separately by any vendor or the customer could resell the deliverable on a standalone basis, (2) there is objective and reliable evidence of the fair value of the undelivered item(s), (3) if the arrangement includes a general right of return, delivery or performance of the undelivered item(s) is considered probable and substantially in the control of the vendor, (4) arrangement consideration should be allocated among the separate units of accounting based on their relative fair values. The amount allocated to the delivered item(s) is limited to the amount that is not contingent on the delivery of additional items or meeting other specified performance conditions, and (5) applicable revenue recognition criteria should be considered separately for separate units of accounting. The Company does not believe EITF 00-21 will have a material impact on its results of operations or financial position.

(m) Concentration of Credit Risk

Financial instruments that subject the Company to credit risk primarily consist of cash and cash equivalents and short-term and long-term investments. The Company's credit risk is managed by investing its

cash and cash equivalents and marketable securities in highly rated money market instruments and debt securities. Due to these factors, no significant additional credit risk is believed by management to be inherent in the Company's assets. As of December 31, 2002, approximately 100% of the Company's cash, cash equivalents, and investments are held at one financial institution.

(3) Accrued Expenses

At December 31, 2002 and 2001, accrued expenses consist of the following:

	December 31	
	2002	2001
Payroll and related costs	$200,308	$ 153,551
Accrued expenses related to issuance of stock (Note 7(a))	—	362,561
Other	627,919	505,548
	$828,227	$1,021,660

(4) Property and Equipment

At December 31, 2002 and 2001, net property and equipment consists of the following:

	December 31	
	2002	2001
Leasehold improvements	$ 399,359	$ 170,287
Laboratory equipment and other	1,715,587	2,781,141
Total property and equipment, at cost	2,114,946	2,951,428
Less: Accumulated depreciation and amortization	1,580,182	2,808,130
Property and equipment, net	$ 534,764	$ 143,298

For the year ended December 31, 2002, laboratory equipment and other includes approximately $113,000 of office equipment financed under capital leases with accumulated depreciation of approximately $11,000. During 2002 and 2001, the Company wrote off unused, fully depreciated property and equipment that had a cost of approximately $1,321,000 and $2,526,000, respectively. A small portion of the equipment was sold in 2001 resulting in a gain of $45,560.

Depreciation expense, which includes amortization of assets recorded under capital leases, was approximately $93,000, $38,000 and $115,000 in 2002, 2001 and 2000, respectively.

(5) Note Receivable from Officer

At December 31, 1999, the Company had a note receivable and accrued interest from a former officer of approximately $270,000, with an interest rate of 6.0% per annum. The Company forgave the note in 2000 and charged this amount to general and administrative expense.

(6) Long-Term Debt

(a) Note Payable

During 1998, the Company entered into a $6.0 million note payable with Founders Financial Group, L.P. (Founders), formerly Forum Capital Markets, L.L.C. and several other investors. The terms of the note payable were as follows: (i) the maturity was November 30, 2003; (ii) the interest rate was 8%; (iii) interest

was payable monthly in arrears, with the principal due in full at maturity of the loan; (iv) the note payable was convertible, at the holders' option, in whole or in part, into shares of common stock at a conversion price equal to $2.40 per share, a premium to fair value at date of issuance, and (v) the note required minimum liquidity, as defined, of $2.0 million. At December 31, 2000, the Company classified the $6.0 million outstanding balance as a current liability because it did not have the financing to remain in compliance with the financial covenants at that time.

On March 28, 2001, the Company entered into an agreement with the noteholders whereby it paid $3.0 million out of the proceeds of the sale of its MethylGene shares discussed in Note 8, to the noteholders in partial satisfaction of the note. The Company also deposited the sum of $821,250 in a money market fund for the purpose of securing payment of the balance remaining on notes. This arrangement was made to encourage the holders of these notes to release their security interest in the shares of MethylGene, Inc. In addition, the Company agreed to reduce the conversion price of the note from $2.40 to $1.50 upon completion of the sale of 60% of the Company's holdings in MethylGene. The Company also agreed to further reduce the conversion price from $1.50 to $0.50 if the balance of the note was not paid in full by the Company before September 30, 2001. Pursuant to Emerging Issues Task Force Issue No. 98-5 (EITF 98-5) *Accounting for Convertible Securities with Beneficial Conversion Features or Contingently Adjustable Conversion Ratios* and EITF 00-27, *Application of Issue No. 98-5 to Certain Convertible Instruments,* since the Company had both the intent and ability to pay the remaining notes prior to September 30, 2001, the Company would measure and recognize any potential beneficial conversion amount only if the Company surrendered its unilateral right to avoid the reduction in the conversion price to $0.50. On September 27, 2001, the Company paid off the remaining $3.0 million to the holders in full satisfaction of the notes. The sum of $821,250 previously deposited to secure the notes held was released to the Company. Since the closing trading price of the Company's common stock was $0.56 per share on March 28, 2001, the date of the reduction in the conversion price, this change did not represent a beneficial conversion feature that would require current or subsequent accounting pursuant to Emerging Issues Task Force 98-5, *Accounting for Convertible Securities with Beneficial Conversion Features or Contingently Adjustable Conversion Ratios* or EITF 00-27, *Application of Issue No. 98-5 to certain Convertible Instruments.*

(b) 9% Convertible Subordinated Notes Payable

Under the terms of the 9% Convertible Subordinated Notes Payable (the 9% Notes), the Company must make semi-annual interest payments on the outstanding principal balance through the maturity date of April 1, 2004. The 9% Notes are convertible at any time prior to the maturity date at a conversion price equal to $35.0625 per share. Upon a change of control of the Company, as defined, the Company will be required to offer to repurchase the 9% Notes at 150% of the original issue price. As of December 31, 2002 and 2001, $1,306,000 of the 9% Notes was outstanding.

(c) 8% Convertible Notes Payable

In March 2000, the Company completed an offering of 8% Convertible Notes Payable (the 8% Notes). As of December 31, 2000, the Company had received approximately $7.6 million with respect to the 8% Notes. Under the terms of the 8% Notes, the Company had to make semiannual interest payments on the outstanding principal balance through the maturity date of November 30, 2002. If the 8% Notes were prepaid before the maturity date, all noteholders were entitled to receive a warrant to purchase the number of shares of common stock equal to the number of shares of common stock that would be issued using the Conversion Ratio. The 8% Notes were convertible at any time prior to the maturity date at a conversion price equal to $0.60 per share of common stock, subject to adjustment under specified circumstances, as defined.

In addition, in connection with the issuance of the 8% Notes, the holders of the $6.0 million note payable (see Note 6(a)) received a warrant to purchase 2,750,000 shares of the Company's common stock at $0.60 per share. The warrant was granted as consideration to the holders of the $6.0 million note for relinquishing their seniority upon liquidation of the Company to the holders of the 8% Notes. The Company computed the value of the warrants to be $547,328, using the Black-Scholes option-pricing model. The Company recorded the $547,328 as a deferred financing cost, which was being amortized to interest expense over the term of the 8% Notes.

On July 10, 2000, the holders of the 8% Notes entered into an amendment to the Subordination and Intercreditor Agreement whereby all parties agreed to release their lien on the assets that were conveyed in the HSP sale (see Note 14). In return for this partial release, the Company agreed that it would set aside $5.0 million from the proceeds with which it would purchase a money market instrument and pledge the same as collateral to secure its obligation to the holders of the 8% Notes. The amount of the pledge was to be reduced as the Company's obligations were converted to equity or repaid.

On March 5, 2001, the Company made an offer to the holders of its 8% Notes to exchange their notes in a ratio of one share of a newly-designated class of Series B Convertible Preferred Stock (Series B Preferred Stock) for each $100 in principal amount of notes tendered. On March 30, 2001, holders of $7.6 million of the Company's 8% Notes exchanged their notes for 76,046 shares of Series B Preferred Stock. The Company recorded an extraordinary loss of $1.4 million related to the early extinguishment of the 8% Notes. The extraordinary loss represents the difference between the carrying value of the 8% Notes and the fair value of the Series B Preferred Stock, as determined by the fair market value of the common stock into which the Series B Preferred Stock was convertible and the write-off of deferred financing costs and related legal fees.

As a result of the exchange, the holders of the 8% Notes released their claim on $5.0 million of the HSP Sale proceeds, which was held as collateral prior to the exchange.

Prior to December 31, 2001, approximately $456,000 of the remaining 8% Notes were converted into 1,140,448 shares of common stock and all of the 78,259 shares of Series B Preferred Stock were converted into 19,564,500 shares of common stock. These conversions were based on a reduced conversion price of $0.40 per share which was agreed to with the holders of Series B Preferred Stock and 8% Note holders as part of the Company's early exercise program discussed in Note 10. In accordance with SFAS No. 84, *Induced Conversions of Convertible Debt,* the Company recorded a charge to interest expense of approximately $353,000. The charge was equal to the fair value of the common stock received less the fair value of common stock that would have been received pursuant to the original conversion terms of the 8% Notes.

Upon maturity of the 8% Notes on November 30, 2002, $31,582 of the remaining 8% Notes plus accrued interest were converted into 52,637 shares of common stock. The Company paid approximately $284,000 to the holders of the remaining 8% Notes in payment of the outstanding principal and accrued interest thereon.

(d) Related Party Notes Payable

In connection with the exchange of shares of Series B preferred stock for 8% Notes in 2001, the Company converted a promissory note payable to a former officer of the Company with a balance of $196,897 into shares of Series B Preferred Stock and subsequently into shares of common stock on terms identical to those described above.

(e) $2.0 Million Line of Credit

On May 30, 2000, the Company entered into a $2.0 million line of credit agreement, available through September 30, 2000, in order to provide working capital until the closing of the HSP sale. The Company drew

down approximately $1.0 million through August 10, 2000. As a condition of the credit agreement, the Company agreed to issue the following warrants to purchase the following number of shares of common stock at an exercise price of $1.08 per share: (i) 500,000 shares to persons designated by Pillar Investments Ltd., a company controlled by a director of the Company, and (ii) 1,000,000 shares to the lenders, proportionate to their respective interests in the $2.0 million line of credit. The Company computed the value of the warrants to be $731,136, using the Black-Scholes option-pricing model and amortized this amount to interest expense over the term of the $2.0 million line of credit.

Following the close of the HSP sale, in October 2000 the Company paid the lenders approximately $0.8 million in cash and issued to the lenders 214,043 shares of common stock having a value of $1.08 per share, pursuant to the terms of the line of credit. The Company has no additional borrowing capacity under this line of credit.

(7) Collaboration and License Agreements

(a) Collaboration and License Agreement with Isis Pharmaceuticals, Inc.

On May 24, 2001, the Company and Isis Pharmaceuticals, Inc. (Isis) entered into a Collaboration and License Agreement (the Isis Agreement). Under the Isis Agreement, the Company granted Isis a license, with the right to sublicense, to the Company's antisense chemistry and delivery patents and patent applications. Isis also agreed to pay the Company a portion of specified sublicense income it receives from specified types of sublicenses of our patents and patent applications. The Company has retained the right to use the patents and patent applications in its own drug discovery and development efforts and in collaboration with third parties. In consideration of the license granted by the Company, Isis paid $15.0 million in cash and issued 857,143 shares of its common stock having an aggregate fair market value on the dates on which title to the shares was received of $17.3 million. An additional $4.5 million installment was due in 2003, subject to possible acceleration depending on the price of Isis' common stock. The remaining number of shares of Isis stock issuable to Hybridon was based on specified market conditions, as defined in the Isis Agreement, and was intended to have a fair market value of $4.5 million.

Following the receipt of 357,143 shares from Isis in September 2001, the Company entered into a number of hedging contracts to protect against a decline in value of the Isis stock while the Company awaited registration of these shares which was necessary before the Company could sell the Isis stock. In accordance with SFAS No. 133, these hedging contracts were derivative instruments and were marked to fair market value with the corresponding changes in fair value recognized in earnings. In accordance with SFAS No. 115, the Company recorded an unrealized loss on the shares of approximately $902,000 prior to entering into these hedging contracts. On November 1, 2001, the Company received an additional 500,000 shares of Isis common stock. The Company did not enter into any hedging contracts in connection with the receipt of these shares and recorded a realized loss of approximately $457,000 on the sale of these shares. In addition, the $306,000 in fees associated with the execution of the hedging contracts was also charged to expenses during 2001. As a result, the Company incurred a net loss of $1,665,000 upon the sale of the Isis shares in November 2001 that is included in Gain on sale of securities, net in the accompanying consolidated statement of operations.

Isis granted the Company a license to use specified antisense patents and patent applications, principally Isis' suite of RNase H patents. The Company has the right under the Isis Agreement to use these patents and patent applications in its drug discovery and development efforts and in specified types of collaborations with third parties. In consideration of this license, the Company originally agreed to pay Isis a total of $6.0 million in cash or in shares of its common stock in three equal annual installments of $2.0 million beginning in 2002. In May, the Company made its first installment tranche payment to Isis consisting of approximately $716,000 in cash and 1,005,499 shares of common stock having a fair market value of approximately $1.2 million on the date of issuance. The Company also agreed to pay Isis a nominal annual maintenance fee and a modest royalty

on sales of products covered by specified patents and patent applications sublicensed to the Company by Isis. The actual number of shares of Hybridon stock that was issuable to Isis under the Isis Agreement was based on certain market conditions, as defined in the Isis Agreement, but was intended to have a fair market value of $6.0 million, if the stock remained in a certain price range as defined in the Isis Agreement.

Prior to the amendment, the Company interpreted its obligations under the Isis Agreement not to be inconsequential and perfunctory. As a result, for the year ended December 31, 2001, the Company recognized revenue over the 10-year term of the Isis Agreement expiring in 2011. Deferred revenue on the accompanying consolidated condensed balance sheet for the year ended December 31, 2001 primarily related to the unrecognized portion of the $32.3 million of cash and Isis stock received by the Company in 2001, the unrecognized portion of the $2.4 million of direct expenses related to the Agreement, and the amortization of the $6.0 million estimated value of all payments to be made by the Company to Isis.

On August 14, 2002, the Company and Isis entered into an amendment to the Isis Agreement. As part of the amendment, each party agreed to cancel the remaining tranche payments due to the other. In addition, the Company and Isis agreed to more specifically define and limit each party's future collaborative obligations under the Isis Agreement. As a result of this amendment, the Company was able to specifically limit the nature of its obligation and related cost of compliance under the Isis Agreement. As a result, the Company has determined that such amended obligation and cost will be inconsequential. In accordance with SAB101, the Company immediately recognized all previously deferred revenue under the Isis Agreement. Revenue for the year ended December 31, 2002 includes $29.5 million of Isis revenue, which is comprised of the net unrecognized portion of the $32.3 million of cash and Isis stock received by the Company in 2001 and the $1.9 million in cash and Company stock paid, less amounts accrued, to Isis by the Company in May 2002. General and Administrative expenses for the year ended December 31, 2002 include the $2.2 million previously unrecognized portion of the $2.4 million in direct expenses related to the Isis Agreement.

(b) Collaboration and License Agreement with Aegera Therapeutics Inc.

On September 13, 2002, the Company and Aegera Therapeutics Inc. entered into a Collaboration and License Agreement (the Collaboration) to research, develop, and optimize a 2nd generation antisense drug targeted to the XIAP gene, which has been implicated in the resistance of cancer cells to chemotherapy. In addition, Hybridon licensed to Aegera, on a non-exclusive basis, rights to the Company's portfolio of 2nd generation antisense chemistries and oral antisense delivery intellectual property owned or licensed by the Company. In consideration for research, development and optimization work to be performed by the Company under the Collaboration and the license of technology by the Company, Aegera paid the Company an upfront license fee and a prepaid milestone. In addition, Aegera agreed to pay the Company additional research payments, milestone payments upon the achievement of specified milestones, and royalties on product sales and sublicensing, if any. Future anticipated payments under the Collaboration could total approximately $8.0 million if all of the milestones are achieved. Aegera is responsible for the development costs of the drug candidate.

(c) Collaboration and License Agreement with Micrologix Biotech Inc.

On September 11, 2002, the Company and Micrologix Biotech Inc. entered into a Collaboration and License Agreement to develop an antisense drug candidate for the treatment of human papillomavirus (HPV). Hybridon licensed Micrologix the exclusive worldwide rights to a family of patents covering a number of antisense oligonucleotides targeted to the HPV genome and non-exclusive rights to a portfolio of antisense chemistries owned or licensed by the Company. In consideration, Micrologix agreed to pay the Company 1) a license fee, 2) milestone payments upon the achievement of specified milestones, and 3) royalties on product sales and sublicensing, if any. The total license fee and milestone payments could total approximately $6.0

million, if all the milestones are achieved. The Company and Micrologix entered into a stock purchase agreement relating to the payment of milestone payments under which Micrologix issued to the Company, without further consideration, shares of preferred stock of Micrologix. Upon the achievement of a milestone, a portion of the shares of preferred stock would, at the option of Micrologix, either (i) be converted into common stock of Micrologix at a conversion rate based on an average market price or (ii) be redeemed by Micrologix for a cash amount equal to the milestone. In a separate transaction with OriGenix Technologies, Inc., Micrologix purchased certain clinical and pre-clinical data and other rights to ORI 1001, a drug candidate formerly under development by OriGenix, a Canadian company dissolved in August 2002 (Note 9). ORI 1001 was initially discovered by the Company and is in phase 1 clinical study for the treatment of diseases associated with HPV. Micrologix has assumed responsibility for development costs of ORI 1001 and has renamed the drug candidate MBI 1121.

(d) License Agreement with University of Massachusetts Medical Center

The Company has a licensing agreement with the University of Massachusetts Medical Center (UMass), under which the Company has received exclusive licenses to technology in specified patents and patent applications. The Company is required to make royalty payments based on future sales of products employing the technology or falling under claims of a patent, as well as a specified percentage of sublicense income received related to the licensed technology. Additionally, the Company is required to pay an annual maintenance fee through the life of the patents. As a result of the Agreement with Isis Pharmaceuticals, Inc. (Note 7(a)), in 2001 the Company paid UMass approximately $1,177,000 based on the consideration received from Isis, less the fair value of the Hybridon stock to be issued to Isis.

(8) Investment in MethylGene Inc.

In January 1996, the Company and institutional investors formed a Quebec company, MethylGene Inc., to develop and market specified compounds and procedures to be agreed upon by the Company and MethylGene.

The Company granted to MethylGene exclusive, royalty-free worldwide licenses to the Company's antisense patents, patent applications and technology to assist in product development.

For these licenses and approximately $734,000, the Company acquired a 49% interest in MethylGene and certain Canadian investors acquired the remaining 51% interest for a total of approximately $5,500,000. Subsequently, MethylGene raised additional proceeds from outside investors that reduced the Company's ownership interest to 22%.

In 2001, the Company sold its ownership interest in MethylGene for total proceeds of approximately $7.2 million (US), which was reduced by approximately $300,000 in professional fees. The Company recorded a net gain of approximately $6.9 million included in gain on sale of securities, net in the accompanying consolidated statement of operations.

(9) OriGenix Technologies, Inc.

In January 1999, the Company and institutional investors formed a Quebec company, OriGenix, to develop and market drugs for the treatment of infectious diseases. Hybridon received a 49% interest in OriGenix in exchange for specified research and development efforts previously undertaken by the Company that were made available to OriGenix and licensed specified antisense compounds and other technology to OriGenix. Subsequently, OriGenix raised additional funds from institutional investors that reduced the Company's ownership interest to 28%. The Company accounted for its investment in OriGenix under the equity method, and reduced such investment to zero at December 31, 2001 due to OriGenix's operating loss.

During 2000, the Company recognized $10,000 of service revenue from sales of DNA products to OriGenix. Prior to the sale of its HSP business (see Note 14), the Company supplied OriGenix with its synthetic DNA needs. During 2000, the Company recognized approximately $90,000 of product revenue from sales to OriGenix in discontinued operations. Also, the Company sold OriGenix a worldwide, royalty-free, paid-up license to manufacture their compounds.

In August 2002, OriGenix filed for bankruptcy in Canada. Upon such filing, the licensing agreement was terminated in accordance with its terms. The Company subsequently licensed the technology it had originally licensed to OriGenix to Micrologix Biotech, Inc. as part of a collaboration agreement with Micrologix (see Note 7(c)).

(10) Stockholders' Equity

(a) Common Stock

At the June 19, 2002 Annual Meeting, the Company's stockholders approved an amendment to the Company's Restated Certificate of Incorporation increasing the number of authorized shares of the Company's Common Stock from 100,000,000 shares to 150,000,000 shares.

Pursuant to the terms of a unit purchase agreement dated as of May 5, 1998, the Company issued and sold a total of 9,597,476 shares of common stock (the "Put Shares") at a price of $2.00 per share. Under the terms of the unit purchase agreement, the initial purchasers (the "Put Holders") of the Put Shares have the right (the "Put Right") to require the Company to repurchase the Put Shares. The Put Right may not be exercised by any Put Holder unless: 1) the Company liquidates, dissolves or winds up its affairs pursuant to applicable bankruptcy law, whether voluntarily or involuntarily; 2) all of the Company's indebtedness and obligations, including without limitation the indebtedness under the Company's then outstanding notes, has been paid in full; and 3) all rights of the holders of any series or class of capital stock ranking prior and senior to the common stock with respect to liquidation, including without limitation the Series A convertible preferred stock, have been satisfied in full. The Company may terminate the Put Right upon written notice to the Put Holders if the closing sales price of its common stock exceeds $4.00 per share for the twenty consecutive trading days prior to the date of notice of termination. Because the Put Right is not transferable, in the event that a Put Holder has transferred Put Shares since May 5, 1998, the Put Right with respect to those shares has terminated. As a consequence of the Put Right, in the event the Company is liquidated, holders of shares of common stock that do not have Put Rights with respect to such shares may receive smaller distributions per share upon the liquidation than if there were no Put Rights outstanding.

As of December 31, 2002, 5,467,686 of the Put Shares continued to be held in the name of Put Holders. On February 14, 2003, the Company repurchased 2,415,880 of these Put Shares (see Note 18). The Company cannot determine at this time whether the Put Rights with respect to the balance of the Put Shares have terminated.

(b) Early Exercise Program

In 2001, the Company effected an "early exercise" program (the Early Exercise Program) to exchange its Series B Preferred Stock, several classes of its warrants, and its remaining 8% Notes for shares of the Company's common stock, in order to simplify the Company's capital structure and to reduce the number of outstanding securities which are exercisable for or convertible into shares of its common stock. The Company offered the holders of its Series B shares the right to convert such shares into common stock at a lower conversion price than that set forth in the Certificate of Designation governing the terms of their Series B shares. The Company offered the holders of various warrants the opportunity to immediately exercise their warrants for the purchase of shares covered by such warrants at a reduced exercise price, either by paying the

lower exercise price for such shares in cash or by engaging in a "cashless" transaction, whereby they could receive a reduced number of shares of common stock in exchange for warrants of equivalent value. The value of the warrants was determined by the Company based on advice from the Company's investment bankers. The Company offered the holders of its remaining 8% Notes the opportunity to exchange the 8% Notes for shares of the Company's common stock at a reduced conversion price. The results of the program are as follows:

- All holders of the Company's Series B Convertible Preferred Stock exchanged their shares for 19,564,500 shares of the Company's common stock;
- Holders of warrants priced between $0.60 and $2.40 exchanged their warrants for 4,669,808 shares of the Company's common stock; and
- $456,221 in 8% notes was exchanged for 1,140,448 shares of common stock.

In accordance with SFAS No. 84, *Induced Conversions of Convertible Debt,* the Company recorded a charge to accumulated deficit of approximately $4,100,000 in connection with the conversion of Series B Preferred Stock. The charge was equal to the fair value of the common stock received less the fair value of common stock that would have been received pursuant to the original conversion terms of the Series B Preferred Stock. This charge was recorded as accretion of preferred stock dividends on the accompanying statement of operations and as a component of the net loss available to common stockholders.

In accordance with SFAS No. 123, *Accounting for Stock-Based Compensation,* the Company did not record any charges related to the warrant exchange as the fair value of the warrants immediately prior to the exchange was equal to the fair value of the common stock issued to the holders as settlement of the warrants. See Note 6(c) for the accounting for the conversion of the 8% Notes.

(c) Warrants

The Company has the following warrants outstanding and exercisable for the purchase of common stock at December 31, 2002:

Expiration Date	Shares	Weighted Exercise Price Per Share
May 4, 2003	3,260,731	$4.10
November 30, 2003	173,333	3.00
March 31, 2006	500,000	0.50
January 1, 2007	100,000	1.65
	4,034,064	
Weighted average exercise price per share		$3.55

Substantially all of such warrants expiring in 2003 were issued in connection with various equity and debt financings described herein. In 2001, the Company issued warrants to purchase 500,000 shares of common stock to an individual who provided consulting services to the Company related to the Isis Agreement. The Company valued these warrants using the Black Sholes pricing model. The warrants' fair value of approximately $570,000 was accounted for as a direct cost of the Isis Agreement (see Note 7(a)). During 2002, the Company issued warrants to purchase 100,000 shares of common stock to a financial advisor which were valued at approximately $98,000 using the Black Sholes pricing model and were charged to general and administrative expense during the year.

(d) Stock Options

The 1990 Stock Option Plan provided for the grant of incentive stock options and nonqualified stock options. All options granted under this plan are fully vested. In October 1995, the Company terminated the issuance of additional options under the 1990 Option Plan. As of December 31, 2002, options to purchase a total of 152,200 shares of common stock remained outstanding under the 1990 Option Plan.

The 1995 Stock Option Plan provides for the grant of incentive stock options and nonqualified stock options. Options granted under this plan generally vest over three to five years, and expire no later than 10 years from the date of grant. A total of 700,000 shares of common stock may be issued upon the exercise of options granted under this plan. The maximum number of shares with respect to which options may be granted to any employee under the 1995 Option Plan shall not exceed 500,000 shares of common stock during any calendar year. The Compensation Committee of the Board of Directors has the authority to select the employees to whom options are granted and determine the terms of each option, including (i) the number of shares of common stock subject to the option; (ii) when the option becomes exercisable; (iii) the option exercise price, which in the case of incentive stock options must be at least 100% and 110% in the case of incentive stock options granted to a stockholder owning in excess of 10% of the Company's common stock, of the fair market value of the common stock as of the date of grant and (iv) the duration of the options which in the case of incentive stock options may not exceed 10 years. As of December 31, 2002, options to purchase a total of 438,516 shares of common stock remained outstanding under the 1995 Stock Option Plan.

Under the 1995 Director Stock Option Plan, a total of 400,000 shares of common stock may be issued upon the exercise of options. Under the terms of the Director Plan options to purchase 5,000 shares of common stock are granted to each eligible director on May 1 of each year and upon appointment to the Board. All options vest on the first anniversary of the date of grant or, in the case of annual options, on April 30 of each year with respect to options granted in the previous year. As of December 31, 2002, options to purchase a total of 168,000 shares of common stock remained outstanding under the Director Plan.

Under the 1997 Stock Incentive Plan, options generally vest over three to five years, and expire no later than 10 years from the date of grant. A total of 13,500,000 shares of common stock may be issued upon the exercise of options granted under the plan. The maximum number of shares with respect to which options may be granted during any calendar year to any employee under the 1997 Stock Incentive Plan is determined by dividing 1,500,000 by the fair market value of a share of the Company's common stock at the time of grant, and may not exceed an overall per participant annual limit of 5,000,000 shares. The Compensation Committee of the Board of Directors has the authority to select the employees to whom options are granted and determine the terms of each option, including (i) the number of shares of common stock subject to the option; (ii) when the option becomes exercisable; (iii) the option exercise price, which in the case of incentive stock options must be at least 100% (110% in the case of incentive stock options granted to those holding 10% or more of the voting power of the Company) of the fair market value of the common stock as of the date of grant and (iv) the duration of the option, which in the case of incentive stock options may not exceed 10 years. As of December 31, 2002, options to purchase a total of 7,311,251 shares of common stock remained outstanding under the 1997 Stock Incentive Plan.

As of December 31, 2002, 4,545,412 options remain available for grant under the 1995 Stock Option Plan, the 1995 Director Plan and the 1997 Stock Incentive Plan.

Stock option activity for the years ended December 31, 2002, 2001, and 2000 is summarized as follows:

	Number of Shares	Exercise Price Per Share	Weighted Average Price Per Share
Outstanding, December 31, 1999	5,389,550	$0.50 – $ 2.00	$0.50
Granted	1,351,026	0.50 – 3.75	1.18
Exercised	(335,240)	0.50	.50
Terminated	(1,003,503)	0.50 – 57.85	.82
Outstanding, December 31, 2000	5,401,833	0.50 – 2.00	0.67
Granted	9,515,987	0.50 – 1.18	0.78
Exercised	(295,907)	0.50 – 0.56	0.50
Terminated	(144,799)	0.50 – 0.56	0.51
Outstanding, December 31, 2001	14,477,114	0.50 – 2.00	0.74
Granted	786,500	0.50 – 1.54	0.92
Exercised	(889,687)	0.50 – 0.56	0.50
Terminated	(66,667)	0.50 – 2.00	0.51
Outstanding, December 31, 2002	14,307,260	$0.50 – $ 2.00	$0.77
Exercisable, December 31, 2000	3,980,476	$0.50 – $ 1.25	$0.60
Exercisable, December 31, 2001	6,913,118	$0.50 – $ 2.00	$0.71
Exercisable, December 31, 2002	8,739,045	$0.50 – $ 2.00	$0.74

	Options Outstanding			Options Exercisable	
Exercise Prices	Number	Weighted Average Remaining Contractual Life (Years)	Weighted Average Exercise Price Per Share	Number	Weighted Average Exercise Price Per Share
$ 0.50	2,820,206	5.49	$0.50	2,777,725	$0.50
0.56	2,519,817	8.24	0.56	1,609,209	0.56
0.71 – 0.83	3,423,000	8.81	0.80	1,390,749	0.77
0.84	3,152,500	8.56	0.84	787,500	0.84
0.93 – 2.00	2,391,737	7.74	1.16	2,173,862	1.14
	14,307,260	7.82	$0.77	8,739,045	$0.74

In accordance with EITF No. 96-18, *Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling Goods or Services*, the Company measures the fair value of non-employee options as they vest using the Black-Scholes option pricing model. The Company has recorded compensation expense of $2,079, $13,516 and $217,701 in 2002, 2001 and 2000, respectively, related to grants to non-employees.

In 1996, the Company granted stock options to a vendor and capitalized the fair value of such options as deferred compensation to be amortized in the future in accordance with SFAS 123, *Accounting for Stock-Based Compensation*. The stock options were to vest based upon the vendor achieving certain performance-based milestones. In 2000, the Company determined that the vendor would not achieve any additional milestones and reversed the unvested deferred compensation of $449,665.

(e) Employee Stock Purchase Plan

In October 1995, the Company adopted the 1995 Employee Stock Purchase Plan (the Purchase Plan), under which up to 100,000 shares of common stock may be issued to participating employees of the Company, as defined, or its subsidiaries. Participation is limited to employees that would not own 5% or more of the total combined voting power or value of the stock of the Company after the grant.

On the first day of a designated payroll deduction period, the "Offering Period", the Company will grant to each eligible employee who has elected to participate in the Stock Purchase Plan an option to purchase shares of common stock as follows: the employee may authorize an amount, a whole percentage from 1% to 10% of such employee's regular pay, to be deducted by the Company from such pay during the Offering Period. On the last day of the Offering Period, the employee is deemed to have exercised the option, at the option exercise price, to the extent of accumulated payroll deductions. Under the terms of the Stock Purchase Plan, the option price is an amount equal to 85% of the fair market value per share of the common stock on either the first day or the last day of the Offering Period, whichever is lower. In no event may an employee purchase in any one Offering Period a number of shares that is more than 15% of the employee's annualized base pay divided by 85% of the market value of a share of common stock on the commencement date of the Offering Period. The Compensation Committee may, in its discretion, choose an Offering Period of 12 months or less for each of the Offerings and choose a different Offering Period for each Offering.

On September 1, 2002, the Company commenced a three month offering period ending November 29, 2002. The Purchase Plan is scheduled to continue throughout 2003, with offering periods commencing on March 1, June 1, September 1, and December 1. In 2002, the Company issued 25,185 shares of common stock under the Purchase Plan.

(f) Repricing

In September 1999, the Company's Board of Directors authorized the repricing of options to purchase 5,251,827 shares of common stock to $0.50 per share, which represented the market value on the date of the repricing. These options are subject to variable plan accounting, as defined in FASB Interpretation No. 44 (FIN 44). The Company will remeasure the intrinsic value of the repriced options, through the earlier of the date of exercise, cancellation or expiration, at each reporting date. A decrease in the intrinsic value of these options between January 1, 2002 and December 31, 2002 resulted in the credit of approximately $1,297,000 to stock compensation expense for the year ended December 31, 2002. For the year ended December 31, 2001, the Company recognized approximately $1,762,000 as stock compensation expense from repriced options. The Company had not recognized any compensation expense related to the repriced options as of December 31, 2000, as the fair market value of the Company's common stock at December 31, 2000 was below the exercise price of the repriced option.

(g) Preferred Stock

The Restated Certificate of Incorporation of the Company permits its Board of Directors to issue up to 5,000,000 shares of preferred stock, par value $0.01 per share, in one or more series, to designate the number of shares constituting such series, and fix by resolution, the powers, privileges, preferences and relative, optional or special rights thereof, including liquidation preferences and dividends, and conversion and redemption rights of each such series. During 1998, the Company designated 1,500,000 shares as Series A convertible preferred stock. During 2001, the Company designated 85,000 shares as Series B convertible preferred stock. As of December 31, 2002 and 2001, there were no shares of Series B convertible preferred stock authorized or outstanding. As discussed in Note (17), during 2002 the Company designated 100,000 shares of Series C Junior Participating Preferred Stock of which there were no shares issued or outstanding at December 31, 2002.

(h) Series A Convertible Preferred Stock

The rights and preferences of the Series A convertible preferred stock are as follows:

Dividends

The holders of the Series A convertible preferred stock are entitled to receive dividends payable semi-annually in arrears at the rate of 6.5% per annum. Such dividends shall be paid, at the election of the Company, either in cash or additional duly authorized, fully paid and non assessable shares of Series A convertible preferred stock. In calculating the number of shares to be paid with respect to each dividend, the Series A convertible preferred stock shall be valued at $100.00 per share. During 2002 and 2001, respectively, total dividend accretion was approximately $4,246,000 and $4,242,000, representing 42,107 and 40,075 Series A shares, respectively.

Liquidation

In the event of a liquidation, dissolution or winding up of the Company, whether voluntary or involuntary, after payment or provision for payment of debts and other liabilities of the Company, the holders of the Series A convertible preferred stock then outstanding shall be entitled to be paid out of the assets of the Company available for distribution to its stockholders, an amount equal to $100.00 per share plus all accrued but unpaid dividends. If the assets to be distributed to the holders of the Series A convertible preferred stock shall be insufficient to permit the payment of the full preferential amounts, then the assets of the Company shall be distributed ratably to the holders of the Series A convertible preferred stock on the basis of the number of shares of Series A convertible preferred stock held. All shares of Series A convertible preferred stock shall rank as to payment upon the occurrence of any liquidation event senior to the common stock.

Voting

The Consent of at least 50% of all outstanding Series A preferred stockholders is required for any amendments or alterations to the Company's Certificate of Incorporation or the Bylaws to the Company that affect the relative rights, preferences, qualifications, limitations or restrictions of the Series A convertible preferred stock.

Conversion and Redemption

Shares of Series A convertible preferred stock are convertible, in whole or in part, at the option of the holder into fully paid and nonassessable shares of common stock at $4.25 per share, subject to adjustment as defined.

The Company, at its option, may cause the Series A convertible preferred stock to be converted in whole or in part, on a pro rata basis, into fully paid and nonassessable shares of common stock using a conversion price equal to $4.00 per common share if the closing bid price, as defined, of the common stock shall have equaled or exceeded 250% of the conversion price of $4.25, subject to adjustment as defined, for at least 20 trading days in any 30 consecutive trading day period ending three days prior to the date of notice of conversion, such event is referred to as the "Market Trigger."

The Company, at its option, may redeem the Series A convertible preferred stock for cash equal to $100.00 per share plus all accrued and unpaid dividends if the Market Trigger has occurred in the period ending three days prior to the date of notice of redemption.

(11) Commitments and Contingencies

(a) Lease Commitments

The Company leases its headquarters facility on Vassar Street in Cambridge, Massachusetts, under a lease that has a 10-year term, which commenced on May 1, 1997. The Company also has office equipment acquired under capital leases. These leases expire in April 2003.

Future approximate minimum commitments as of December 31, 2002, under existing lease agreements through 2007, are as follows:

December 31,	Operating Leases	Capital Leases
2003	$ 611,000	$34,000
2004	611,000	—
2005	611,000	—
2006	611,000	—
2007	204,000	—
	$2,648,000	$34,000

During 2002, 2001, and 2000, facility rent expense for continuing operations, net of sublease income, was approximately $282,000, $293,000 and $246,000, respectively.

(b) External Collaborations

The Company funds research efforts of various academic collaborators and consultants in connection with its research and development programs. Total future fixed commitments under these agreements approximate $220,000 and $23,000 for 2003 and 2004, respectively.

(c) Related-Party Agreements with Affiliates of Stockholders and Directors

The Company has entered into consulting agreements, stock placement agreements and an advisory agreement with several companies that are controlled by shareholders and directors of the Company including Founders Financial Group, L.P., Pillar S.A., Pillar Investment Limited, and TMC Development. During 2002, 2001 and 2000, the Company paid $107,000, $460,000 and $74,000, respectively, under these agreements with related parties.

(d) Contingencies

From time to time, the Company may be exposed to various types of litigation. The Company is not engaged in any legal proceedings that are expected, individually or in the aggregate, to have a material adverse effect on the Company's financial condition or results of operations. In the fourth quarter of 2002, the United States patent and Trademark Office (PTO) declared an interference involving a patent application exclusively licensed by the Company from UMass and three patents issued to the National Institutes of Health. The PTO's declaration of interference named UMass as the senior party. Under the license agreement with UMass, the Company is acting on behalf of UMass in connection with the interference. The Company is not practicing nor does it intend to practice any of the intellectual property involved in the interference. Consequently, if it is unable to resolve the matter in a way beneficial to the Company, it will not have a negative impact on the Company's business. If UMass is successful in the patent interference, the Company could be entitled to a portion of sublicense income.

(12) Income Taxes

During 2001, the Company accrued $500,000 for Alternative Minimum Tax (AMT) of which $450,000 was paid prior to December 31, 2001. The National Economic Stabilization and Recovery Act, enacted in March 2002, has temporarily rescinded the AMT as it applies to the Company. The Company received a $450,000 refund and recognized a $500,000 credit to operations during 2002 in accordance with SFAS No. 109, *Accounting for Income Taxes*.

The Company applies SFAS No. 109, *Accounting for Income Taxes*. Accordingly, a deferred tax asset or liability is determined based on the difference between the financial statement and tax basis of assets and liabilities, as measured by the enacted tax rates expected to be in effect when these differences reverse. At December 31, 2002, the Company had net operating loss and tax credit carryforwards for federal income tax purposes of approximately $224.0 million and $4.2 million, respectively, available to reduce federal taxable income and federal income taxes, respectively. These carryforwards expire through 2022. The Tax Reform Act of 1986 limits the amount of net operating loss and credit carryforwards that companies may utilize in any one year in the event of cumulative changes in ownership over a three-year period in excess of 50%. The Company has completed several financings since the effective date of the Tax Reform Act of 1986, which as of December 31, 2002, have resulted in ownership changes in excess of 50%, as defined under the Act and which will limit the Company's ability to utilize its net operating loss carryforwards. Ownership changes in future periods may place additional limits on the Company's ability to utilize net operating loss and tax credit carryforwards.

As of December 31, 2002 and 2001, the components of the deferred tax assets are approximately as follows:

	2002	2001
Operating loss carryforwards	$90,275,000	$84,551,000
Tax credit carryforwards	4,158,000	3,991,000
Other	791,000	704,000
	95,224,000	89,246,000
Valuation allowance	(95,224,000)	(89,246,000)
	$ —	$ —

The Company has provided a valuation allowance for its deferred tax asset due to the uncertainty surrounding the ability to realize this asset.

(13) Employee Benefit Plan

The Company has an employee benefit plan under Section 401(k) of the Internal Revenue Code. The plan allows employees to make contributions up to a specified percentage of their compensation. Under the plan, the Company may, but is not obligated to, match a portion of the employees' contributions up to a defined maximum. The Company is currently contributing up to 3% of employee base salary, by matching 50% of the first 6% of annual base salary contributed by each employee. Approximately $58,000, $44,000, and $47,000 of 401(k) benefits were charged to continuing operations during 2002, 2001, and 2000, respectively.

(14) Sale of Hybridon Specialty Products

In September 2000, the Company completed the sale of its Hybridon Specialty Products (HSP) business, which manufactured and marketed oligonucleotides to Avecia Biotechnology, a subsidiary of Avecia, Inc. of Manchester, United Kingdom, for up to $15.0 million. In 2000, the Company recorded a gain

of approximately $6.3 million on the HSP sale, comprised of net proceeds received during 2000 of approximately $12.0 million less transaction and other costs of approximately $1.2 million and the book value of the net assets sold. The transaction costs primarily consist of legal and accounting fees, severance arrangements with certain employees, and other estimated costs associated with consummating the sale. Payment of the remaining $3.0 million was held back by Avecia since, as part of this transaction, the Company had entered into a supply agreement whereby it was committed to make minimum purchases during 2000 and 2001 on a "take or pay" basis if Avecia's third-party sales did not meet specified goals. Hybridon was also required to make quarterly payments to cover purchasing shortfalls, based on an agreed upon formula.

The gain recognized in 2000 on the Asset Sale is computed as follows:

Proceeds		$12,000,000
Property and equipment sold, net	$4,894,887	
Security deposit	90,000	
Net book value of assets sold	4,984,887	
Current liabilities assumed by the buyer	(88,969)	
Long-term liabilities assumed by the buyer	(324,555)	
Net assets sold		(4,571,363)
Transaction and other costs		(1,157,578)
Gain on sale		$ 6,271,059

On September 20, 2001, the Company received the $3.0 million contingent payment in full from Avecia. Upon receipt of the $3.0 million payment, the Company applied approximately $1,032,000 toward the satisfaction of the above mentioned purchasing shortfall and recognized the remaining $1,968,000 as income from the sale of the discontinued operations. In November 2001, the Company also received a refund of approximately $695,000 of the Company's minimum payments to Avecia per the terms of the supply agreement. This refund increased the income from discontinued operations during the year ended December 31, 2001 to approximately $2,663,000.

The consolidated financial statements of the Company for the year ended December 31, 2000 were restated to reflect the financial results of the HSP business as a discontinued operation. Reported revenues, expenses and cash flows exclude the operating results of the discontinued operations. Revenues from discontinued operations for the year ended December 31, 2000 are approximately $2,950,000. The 2000 gain includes the gain on sale as calculated above of $6.3 million, net of an $0.8 million operating loss from discontinued operations.

(15) Income (Loss) Per Share

The following table sets forth the computation of basic and diluted income (loss) per share:

	Years Ended December 31,		
	2002	2001	2000
Numerator:			
Income (loss) from continuing operations	$16,971,540	$ (6,583,924)	$(8,384,753)
Income (loss) from discontinued operation	—	2,662,597	5,462,154
Extraordinary loss	—	(1,411,876)	—
Net income (loss)	16,971,540	(5,333,203)	(2,922,599)
Accretion of preferred stock dividend	(4,246,282)	(8,341,935)	(4,087,317)
Numerator for basic income (loss) applicable to common shareholders	12,725,258	(13,675,138)	(7,009,916)
Effect of dilutive securities:			
Interest expense related to convertible debt	21,896	—	—
Numerator for diluted income (loss) applicable to common shareholders	$12,747,154	$(13,675,138)	$(7,009,916)
Denominator for basic income (loss) per share:			
Weighted average shares outstanding	46,879,232	30,820,098	17,418,233
Effect of dilutive securities:			
Common stock options and warrants	5,647,539	—	—
Convertible debt	457,644	—	—
Denominator for diluted income (loss) per share	52,984,415	30,820,098	17,418,233
Income (loss) per share — basic			
Continuing operations	$ 0.36	$ (0.21)	$ (0.48)
Discontinued operations	—	0.09	0.31
Extraordinary loss	—	(0.05)	—
Net income (loss) per share	0.36	(0.17)	(0.17)
Accretion of preferred stock dividends	(0.09)	(0.27)	(0.23)
Net income (loss) per share applicable to common stockholders	$ 0.27	$ (0.44)	$ (0.40)
Income (loss) per share — diluted			
Continuing operations	$ 0.32	$ (0.21)	$ (0.48)
Discontinued operations	—	0.09	0.31
Extraordinary loss	—	(0.05)	—
Net (income) loss per share	0.32	(0.17)	(0.17)
Accretion of preferred stock dividends	(0.08)	(0.27)	(0.23)
Net income (loss) per share applicable to common stockholders	$ 0.24	$ (0.44)	$ (0.40)

For the year ended December 31, 2002, 22,383,725 shares were not included in diluted net income per share as the effects of certain convertible debt, convertible preferred stock, warrants, and certain stock options are antidilutive. For the years ended December 31, 2001 and 2000, diluted net loss per share from continuing operations is the same as basic net loss per common share, as the effects of the Company's potential common stock equivalents are antidilutive. Total antidilutive securities were 40,714,556 and 49,098,529 for the years ended December 31, 2001 and 2000, respectively, and consist of stock options, warrants, convertible preferred stock and convertible debt instruments (on an as-converted basis).

(16) Supplemental Disclosure of Cash Flow Information

Supplemental disclosure of cash flow information for the periods presented are as follows:

	Years Ended December 31,		
	2002	2001	2000
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 121,278	$ 379,294	$ 641,132
Cash (received) paid for taxes	$ (450,000)	$ 450,000	$ —
Supplemental disclosure of non cash financing and investing activities:			
Exchange of 8% convertible notes payable for Series B preferred stock and common stock	$ 31,582	$ 8,060,779	$ —
Accretion of Series A and Series B preferred stock dividends	$4,246,282	$ 4,241,935	$4,087,317
Dividend from induced conversion of Series B preferred stock	$ —	$ 4,100,000	$ —
Issuance of common stock for services	$ —	$ 140,358	$ —
Interest paid in kind on 8% Notes	$ 27,657	$ 305,180	$ —
Forgiveness of note receivable	$ —	$ —	$ 270,050
Conversion of Series A preferred stock into common stock	$ 92	$ 614	$ 1,821
Conversion of Series B preferred stock into common stock	$ —	$ 19,565	$ —
Conversion of line of credit into common stock	$ —	$ —	$ 231,167
Issuance of stock options to non-employees, net of terminations	$ —	$ 10,756	$ (50,781)
Issuance of warrants in connection with consulting services	$ —	$ 569,667	$ —
Cashless exercise of stock warrants	$ 247	$ 4,443	$ —
Fair value of ISIS stock received	$ —	$17,284,288	$ —
Deferred compensation relating to issuance of stock options	$ 6,150	$ 112,192	$ —
Equipment acquired under capital lease	$ 113,303	$ —	$ —

(17) Shareholder Rights Plan

The Company adopted a shareholder rights plan in December 2001. Under the rights plan, one right was distributed as of the close of business on January 7, 2002 on each then outstanding share of the Company's common stock. The rights will automatically trade with the underlying common stock and ordinarily will not be exercisable. The rights will only become exercisable if a person acquires beneficial ownership of, or commences a tender offer for, 15 percent or more of the Company's common stock, unless, in either case, the transaction was approved by the Company's board of directors.

If the rights become exercisable, the type and amount of securities receivable upon exercise of the rights would depend on the circumstances at the time of exercise. Initially, each right would entitle the holder to purchase one one-thousandth of a share of the Company's newly created Series C Junior Participating Preferred Stock for an exercise price of $13.00. If a person acquires 15 percent or more of the Company's common stock in a transaction that was not approved by the Company's board of directors, then each right, other than those owned by the acquiring person, would instead entitle the holder to purchase $26.00 worth of the Company's common stock for the $13.00 exercise price. If the Company is involved in a merger or other transaction with another company in which the Company is not the surviving corporation, or transfers more than 50% of its assets to another company, in a transaction that was not approved by the Company's board of

directors, then each right, other than those owned by the acquiring person, would instead entitle the holder to purchase $26.00 worth of the acquiring company's common stock for the $13.00 exercise price.

The Company's board of directors may redeem the rights for $0.001 per right at any time until ten business days after a person acquires 15 percent or more of the Company's outstanding common stock. Unless the rights are redeemed or exchanged earlier, they will expire on December 10, 2011.

(18) Subsequent Events

On February 14, 2003, the Company repurchased 4,643,034 shares of its common stock at a price of $1.15 per share from two Middle Eastern stockholders and their affiliates. The fair market value of the common stock was $0.75 per share on the date of the transaction resulting in a premium of approximately $1,857,000 in the aggregate. The Company charged this premium to general and administrative expense in the quarter ending March 31, 2003.

Exhibit Index

Exhibit No.	Description
3.1(1)	Restated Certificate of Incorporation of the Registrant, as amended.
3.2(2)	Amended and Restated Bylaws of the Registrant.
4.1(2)	Specimen Certificate for shares of Common Stock, $.001 par value, of the Registrant.
4.2(3)	Indenture dated as of March 26, 1997 between Forum Capital Markets LLC and the Registrant.
4.3(4)	Certificate of Designation of Series A Preferred Stock, par value $.01 per share, dated May 5, 1998.
4.4(4)	Class A Warrant Agreement dated May 5, 1998.
4.5(4)	Class B Warrant Agreement dated May 5, 1998.
4.6(4)	Class C Warrant Agreement dated May 5, 1998.
4.7(5)	Rights Agreement dated December 10, 2001 by and between the Registrant and Mellon Investor Services LLC, as rights agent.
†10.1(2)	License Agreement dated February 21, 1990 and restated as of September 8, 1993 between the Registrant and University of Massachusetts Medical Center.
†10.2(2)	Patent License Agreement effective as of October 13, 1994 between the Registrant and McGill University.
†10.3(2)	License Agreement effective as of October 25, 1995 between the Registrant and the General Hospital Corporation.
†10.4(2)	License Agreement dated as of October 30, 1995 between the Registrant and Yoon S. Cho-Chung.
†10.5(2)	System Design and Procurement Agreement dated as of December 16, 1994 between the Registrant and Pharmacia Biotech, Inc.
10.6(2)	Registration Rights Agreement dated as of February 21, 1990 between the Registrant, the Worcester Foundation for Biomedical Research, Inc. and Paul C. Zamecnik.
††10.7(2)	1990 Stock Option Plan, as amended.
††10.8(2)	1995 Stock Option Plan.
††10.9(2)	1995 Director Stock Plan.
††10.10(2)	1995 Employee Stock Purchase Plan.
††10.11(18)	Employment Agreement dated April 1, 2002 between the Registrant and Dr. Sudhir Agrawal.
††10.12	Consulting Agreement dated as of March 1, 2003 between the Registrant and Dr. Paul C. Zamecnik.
10.13(6)	Registration Rights Agreement dated as of January 24, 1996 between the Registrant and G.D. Searle & Co.
10.14(3)	Registration Rights Agreement dated as of March 26, 1997 between Forum Capital Markets LLC and the Registrant.
†10.15(8)	Amendment No. 1 to License Agreement, dated as of February 21, 1990 and restated as of September 8, 1993, by and between University of Massachusetts Medical Center and the Registrant, dated as of November 26, 1996.
†10.16(9)	Licensing Agreement dated March 12, 1999 by and between Hybridon, Inc. and Integrated DNA Technologies, Inc.
†10.17(10)	Licensing Agreement dated September 7, 1999 by and between Hybridon, Inc. and Genzyme Corporation.
10.18(11)	License Agreement dated September 20, 2000 by and between Hybridon and Boston Biosystems, Inc.

Exhibit No.	Description
10.19(11)	Assignment of Coexclusive License dated September 20, 2000 by and between Hybridon and the Public Health Service.
10.20(11)	Oligonucleotide Purification Patent License Agreement dated September 20, 2000 by and between Hybridon and Boston Biosystems, Inc.
10.21(12)	Asset Purchase Agreement dated June 29, 2000 by and between Hybridon and Boston Biosystems, Inc.
†10.22(11)	Assignment of Patent Rights dated September 20, 2000 by and between Hybridon and Boston Biosystems, Inc.
†10.23(11)	PNT Monomer Patent License and Option Agreement dated September 20, 2000 by and between Hybridon and Boston Biosystems, Inc.
†10.24(11)	Agreement Relating to Patents Forming Part of Acquired Assets but to be Licensed Back to Hybridon for the Purposes of OriGenix Agreements dated September 20, 2000 by and between Hybridon and Boston Biosystems, Inc.
10.25(13)	Agreement dated March 28, 2001 by and between Hybridon, Founders Financial Group, Pecks Management Partners L.T.D. and General Motors Investment Management Corporation, in its capacity as Trustee for the General Motors Employees Global Trust Group.
10.26(13)	Stock Purchase Agreement by and between Paul Capital Partners L.P. and PCP Associates and Hybridon dated March 30, 2001.
10.27(13)	Agreement and Mutual Release between Hybridon and MethylGene, Inc. dated March 21, 2001.
10.28(14)	Amended and Restated 1997 Stock Incentive Plan.
†10.29(15)	Collaboration and License Agreement by and between Isis Pharmaceuticals, Inc., and Hybridon, Inc., dated May 24, 2001.
10.30(15)	Master Agreement relating to the Cross License of Certain Intellectual Property and Collaboration by and between Isis Pharmaceuticals, Inc. and Hybridon, Inc., dated May 24, 2001.
10.31(15)	Share Purchase Agreement between Hybridon, Inc. and Royal Bank Ventures, Inc., Fonds De Solidarite Des Travailleurs Du Quebec (F.T.Q.), and Ontario Teacher's Pension Plan Board, dated May 11, 2001.
††10.32(16)	Employment Agreement by and between Stephen R. Seiler and the Company effective as of July 25, 2001.
10.33(17)	Unit Purchase Agreement by and among Registrant and certain persons and entities listed therein, dated April 1, 1998.
10.34(17)	Offer to Exchange Hybridon Warrants and Shares of Series B Convertible Preferred Stock, dated July 29, 2001.
10.35(18)	Employment Agreement dated April 1, 2002 between the Registrant and Robert G. Andersen.
10.36(7)	Executive Stock Option Agreement for 3,150,000 Options effective as of July 25, 2001 between the Registrant and Stephen R. Seiler.
10.37(7)	Executive Stock Option Agreement for 490,000 Options effective as of July 25, 2001 between the Registrant and Stephen R. Seiler.
10.38(19)	Executive Stock Option Agreement for 1,260,000 Options effective as of July 25, 2001 between the Registrant and Dr. Sudhir Agrawal.
10.39(19)	Executive Stock Option Agreement for 550,000 Options effective as of July 25, 2001 between the Registrant and Dr. Sudhir Agrawal.
10.40(19)	Executive Stock Option Agreement for 500,000 Options effective as of July 25, 2001 between the Registrant and Dr. Sudhir Agrawal.
10.41(19)	Consulting Agreement effective as of October 1, 2002 between the Registrant and Pillar, S.A.

Exhibit No.	Description
10.42	Amendment No. 1 to the Collaboration and License Agreement, dated as of May 24, 2001 by and between Isis Pharmaceuticals, Inc and the Registrant, dated as of August 14, 2002.
†10.43	License Agreement by and between Louisiana State University and the Registrant, dated July 1, 1998.
23.1	Limitation of Remedies Against Arthur Andersen LLP. Please see Item 9 of this Annual Report on Form 10-K.
23.2	Consent of Ernst & Young LLP.
99.1	Certification of CEO Pursuant to Section 906
99.2	Certification of CFO Pursuant to Section 906

(1) Incorporated by reference to Exhibits to the Registrant's Amendment No. 1 to Form 8-A dated December 21, 2001. (File No. 0-27352)

(2) Incorporated by reference to Exhibits to the Registrant's Registration Statement on Form S-1 (File No. 33-99024).

(3) Incorporated by reference to Exhibits to the Registrant's Current Report on Form 8-K dated April 2, 1997. (File No. 0-27352)

(4) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended March 31, 1998. (File No. 0-27352)

(5) Incorporated by reference to Exhibits to the Registrant's Current Report on Form 8-K filed on December 21, 2001. (File No. 0-27352)

(6) Incorporated by reference to Exhibits to the Registrant's Annual Report on Form 10-K for the year ended December 31, 1995. (File No. 0-27352)

(7) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended June 30, 2002. (File No. 0-27352)

(8) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended June 30, 1997. (File No. 0-27352)

(9) Incorporated by reference to Exhibits to the Registrant's Annual Report on Form 10-K for the year ended December 31, 1998. (File No. 0-27352)

(10) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended September 30, 1999. (File No. 0-27352)

(11) Incorporated by reference to Exhibits to the Registrant's Registration Statement on Form S-1 (File No. 333-69649).

(12) Incorporated by reference to the Registrant's Proxy Statement dated August 8, 2000. (File No. 0-27352)

(13) Incorporated by reference to Exhibits to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2000. (File No. 0-27352)

(14) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended March 31, 2001. (File No. 0-27352)

(15) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended June 30, 2001. (File No. 0-27352)

(16) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended September 30, 2001. (File No. 0-27352)

(17) Incorporated by reference to Exhibits to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2001. (File No. 0-27352)

(18) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended March 31, 2002. (File No. 0-27352)

(19) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the year ended September 30, 2002. (File No. 0-27352)

† Confidential treatment granted as to certain portions, which portions are omitted and filed separately with the Commission.

†† Management contract or compensatory plan or arrangement required to be filed as an Exhibit to the Annual Report on Form 10-K.